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enhanced  
NEWS 4 APR 02 DWPI: New display format ALLSTR available  
NEWS 5 APR 02 New Thesaurus Added to Derwent Databases for Smooth  
Sailing through U.S. Patent Codes  
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NEWS 7 APR 07 CA/CAPLUS CLASS Display Streamlined with Removal of  
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NEWS 10 JUN 16 WPI First View (File WPIFV) will no longer be  
available after July 30, 2010  
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NEWS 14 JUN 21 Removal of Pre-IPC 8 data fields streamline displays  
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of Biofuel Research Reveal China Now Atop U.S. in  
Patenting and Commercialization of Bioethanol  
NEWS 17 JUN 29 Enhanced Batch Search Options in DGENE, USGENE,  
and PCTGEN  
NEWS 18 JUL 19 Enhancement of citation information in INPADOC  
databases provides new, more efficient competitor  
analyses  
NEWS 19 JUL 26 CAS coverage of global patent authorities has  
expanded to 61 with the addition of Costa Rica  
  
NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,  
AND CURRENT DISCOVER FILE IS DATED 07 JULY 2010.

10568655 09/08/2010 STN: SEARCH

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	ENTRY	SESSION
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DICTIONARY FILE UPDATES: 7 SEP 2010 HIGHEST RN 1240243-66-6

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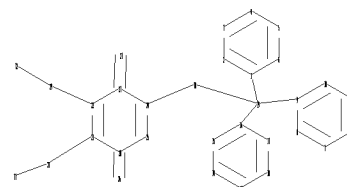
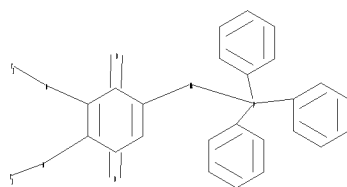
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Uploading C:\Program Files\Stnexp\Queries\GWS.str



chain nodes :

19 26 27 28 29 30 32 33

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 20 21 22 23 24  
25

chain bonds :

1-19 9-19 16-19 19-30 20-26 21-28 22-29 23-27 24-30 28-33 29-32

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18  
14-15 15-16 16-17 17-18 20-21 20-25 21-22 22-23 23-24 24-25

exact/norm bonds :

19-30 20-21 20-25 20-26 21-22 21-28 22-23 22-29 23-24 23-27 24-25 24-30  
28-33 29-32

exact bonds :

1-19 9-19 16-19

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18  
14-15 15-16 16-17 17-18

G1:H,Ak

Match level :

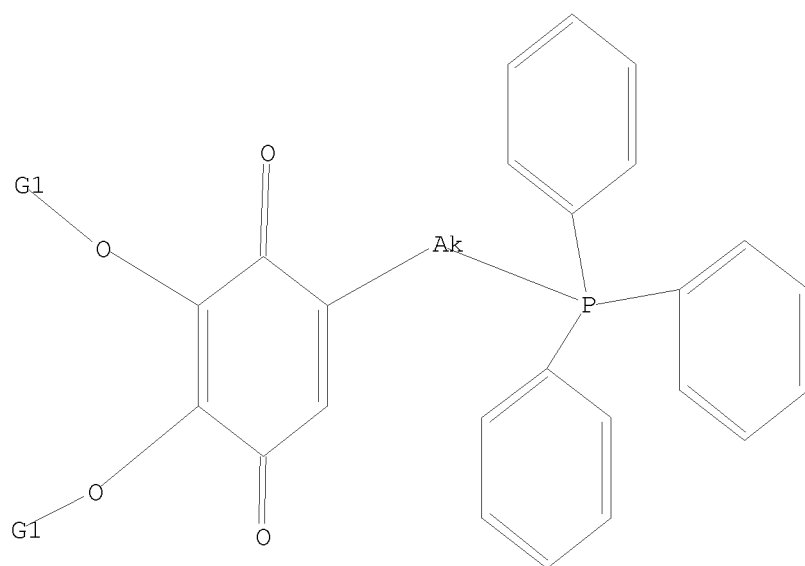
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS  
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:CLASS 28:CLASS  
29:CLASS 30:CLASS 32:CLASS 33:CLASS

L1 STRUCTURE UPLOADED

=> D L1

L1 HAS NO ANSWERS

L1 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> S L1 FULL

FULL SEARCH INITIATED 12:49:39 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 842 TO ITERATE

100.0% PROCESSED 842 ITERATIONS

21 ANSWERS

SEARCH TIME: 00.00.01

L2 21 SEA SSS FUL L1

=> FILE CAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

192.03

192.91

FILE 'CAPLUS' ENTERED AT 12:49:48 ON 08 SEP 2010

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FILE COVERS 1907 - 8 Sep 2010 VOL 153 ISS 11  
 FILE LAST UPDATED: 7 Sep 2010 (20100907/ED)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2010  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2010

CAPLUS now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2010.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L2

L3 73 L2

=> D L3 IBIB ABS HITSTR 1-73

L3 ANSWER 1 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:689488 CAPLUS

DOCUMENT NUMBER: 152:575841

TITLE: Hair coloring method comprising after-treatment with bioquinone-containing conditioner

INVENTOR(S): Reichert, Anja; Rohland, Christa; Kleen, Astrid; Hartwich, Christa

PATENT ASSIGNEE(S): Henkel AG & Co. KGaA, Germany

SOURCE: PCT Int. Appl., 39pp.; Chemical Indexing Equivalent to 152:509153 (DE)  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010060730	A1	20100603	WO 2009-EP64377	20091030
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,			

IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,  
SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,  
ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

DE 102008055615 A1 20100506 DE 2008-102008055615 20081103

PRIORITY APPLN. INFO.:

DE 2008-102008055615A 20081103

AB The invention relates to a method for altering the color of keratin fibers that is kind to said fibers. The method is characterized by a two-stage application and by a combination of specific active ingredients, in particular amino acids containing hydroxyl groups and plant exts. in the colorant preparation and bioquinones in the aftertreatment agent. The invention also relates to a packaging unit comprising colorant preps. of this type and aftertreatment agents. The invention allows significantly improved fiber strength to be achieved in relation to conventional colorants. Thus a hair dye cream contained (weight%): oxidation dye precursors (mixture of weight%: p-toluylenediamine sulfate 66.7; 3-aminophenol 4.5; resorcin 16.7; 4-chlororesorcin 12.1) 1.32; Lanette D 6.60; Lorol C12-18 2.40; Eumulgin B2 0.60; Eumulgin B1 0.60; Lamesoft PO 65 2.00; Akypo Soft 45HP 10.00; Texapon K14 S Special 2.80; Product W 37194 3.75; ammonium sulfate 0.47; sodium sulfite 96% 0.40; ascorbic acid 0.10; HEDP 60% 0.20; sodium silicate 40/43 0.50; L-serine 1.0; ammonia 25% 6.50; perfume q.s.; water to 100. The developer included (weight%): ammonia 25% 0.65; dipicolinic acid 0.10; disodium pyrophosphate 0.03; HEDP, 60% 1.50; Texapon NSO 2.00; Dow Corning DB 110A 0.07; Aculyn 33A 15.00; hydrogen peroxide 50% 12.00; water to 100. The post-treatment composition contained (weight%): isopropylmyristate 1.30; Cutina GMS-V 0.30; Eumulgin B2 0.30; cetearyl alc. 4.60; Dehyquart F75 1.00; Varisoft W 75PG 4.00; stearamidopropyl dimethylamine 0.40; methylparaben sodium 0.30; glycine 0.20; citric acid monohydrate 0.45; Cosmedia CTH 0.50; Hydrotritium WQ 0.50; D-panthenol 75% 0.20; marine hydrolyzed collagen 0.60; ubiquinone-50 0.012 phenoxyethanol 0.40; perfume q.s.; water to 100.

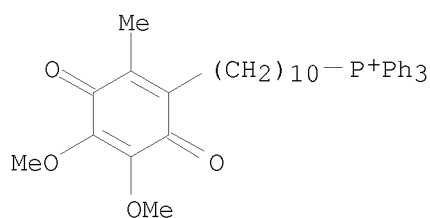
IT 444890-41-9D, Mitoquinone, derivs.

RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)

(hair dyeing method with post-treatment using a bioquinone-containing conditioner)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:628631 CAPLUS

DOCUMENT NUMBER: 152:576351

TITLE: Method for moderately increasing the proton

conductivity of biological membranes with the aid of mitochondria-targeted delocalized cations

INVENTOR(S): Skulachev, Vladimir Petrovich; Skulachev, Maxim Vladimirovich

PATENT ASSIGNEE(S): Limited Liability Company "Mitotechnology", Russia

SOURCE: PCT Int. Appl., 54pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Russian

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010056145	A1	20100520	WO 2008-RU706	20081112
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: WO 2008-RU706 20081112

OTHER SOURCE(S): MARPAT 152:576351

AB The invention relates to the field of biol. and medicine, and in particular can be used in medicine for preparing a pharmaceutical composition for

the specific, self-regulating uncoupling of mitochondria. The invention may be useful for treating diseases and conditions associated with the disruption of cellular metabolism, in the treatment of obesity, including its pathol. forms, and also for treating diseases associated with the increased formation of free radicals and active forms of oxygen. In addition, the invention can be employed in biotechnol. in order to stimulate the growth of yeasts and microorganisms, and also to stimulate the development of tissues and organs of plant and animal origin.

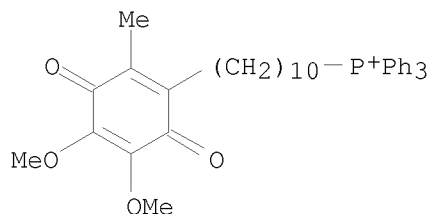
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for moderately increasing the proton conductivity of biol. membranes with the aid of mitochondria-targeted delocalized cations)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:594464 CAPLUS

DOCUMENT NUMBER: 152:568456

TITLE: Preparation of deuterated hydroxyphenylalanine derivatives

INVENTOR(S): Gant, Thomas G.; Hodiluk, Craig; Woo, Soon H.

PATENT ASSIGNEE(S): Auspex Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 95pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

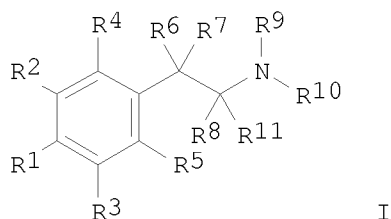
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010054286	A2	20100514	WO 2009-US63685	20091109
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
US 20100172916	A1	20100708	US 2009-614530	20091109
PRIORITY APPLN. INFO.:			US 2008-112788P	P 20081110
OTHER SOURCE(S):	MARPAT 152:568456			
GI				



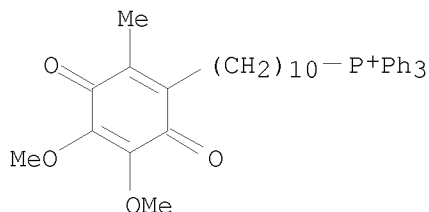


AB The invention relates to new deuterated hydroxyphenylamines and hydroxyphenylalanines I [R1, R2 are H, D, OH, or OD, wherein at least one of R1 and R2 is H or D; R3-R10 are independently H or D; R11 is H, D, CO2H, or CO2D, or CO2R12, where R12 is alkyl or deuterated alkyl; at least one of R1-R12 is deuterium or contains deuterium (with provisos)] and their pharmaceutically-acceptable salts, which are modulators of hormone and/or pigment levels for use in pharmaceutical compns. Thus, L-m-d2-tyrosine was prepared by a multistep sequence starting with cyclocondensation of m-(benzyloxy)benzaldehyde with N-acetylglycine. An in vitro liver microsomal stability assay showed that L-m-d2-tyrosine and L-m-d3-tyrosine showed a decrease in degradation half-life as compared to the non-isotopically enriched drug.

IT 444890-41-9, MitoQ  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dietary supplement; preparation of deuterated hydroxyphenylalanine derivs.)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 4 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:558524 CAPLUS

DOCUMENT NUMBER: 152:509153

TITLE: Hair dyeing method with post-treatment using a bioquinone-containing conditioner

INVENTOR(S): Reichert, Anja; Rohland, Christa; Kleen, Astrid; Hartwich, Christa

PATENT ASSIGNEE(S): Henkel AG & Co. KGaA, Germany

SOURCE: Ger. Offen., 44pp.; Chemical Indexing Equivalent to 152:575841 (WO)  
 CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102008055615	A1	20100506	DE 2008-102008055615	20081103
WO 2010060730	A1	20100603	WO 2009-EP64377	20091030

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

## PRIORITY APPLN. INFO.:

DE 2008-102008055615A 20081103

AB The invention concerns a method to treat hair (a) with an oxidative hair dye composition that contains a fiber structure-improving ingredient, e.g. amino acid or plant extract; (b) waiting period of up-to 60 min; (c) post-treatment with a composition that contains a bioquinone, preferably ubiquinone-50. Thus a hair dye cream contained (weight%): oxidation dye precursors (mixture of weight%: p-toluylenediamine sulfate 66.7; 3-aminophenol 4.5; resorcin 16.7; 4-chlororesorcin 12.1) 1.32; Lanette D 6.60; Lorol C12-18 2.40; Eumulgin B2 0.60; Eumulgin B1 0.60; Lamesoft PO 65 2.00; Akypo Soft 45HP 10.00; Texapon K14 S Special 2.80; Product W 37194 3.75; ammonium sulfate 0.47; sodium sulfite 96% 0.40; ascorbic acid 0.10; HEDP 60% 0.20; sodium silicate 40/43 0.50; L-serine 1.0; ammonia 25% 6.50; perfume q.s.; water to 100. The developer included (weight%): ammonia 25% 0.65; dipicolinic acid 0.10; disodium pyrophosphate 0.03; HEDP, 60% 1.50; Texapon NSO 2.00; Dow Corning DB 110A 0.07; Aculyn 33A 15.00; hydrogen peroxide 50% 12.00; water to 100. The post-treatment composition contained (weight%): isopropylmyristate 1.30; Cutina GMS-V 0.30; Eumulgin B2 0.30; cetearyl alc. 4.60; Dehyquart F75 1.00; Varisoft W 75PG 4.00; stearamidopropyldimethylamine 0.40; methylparaben sodium 0.30; glycine 0.20; citric acid monohydrate 0.45; Cosmedia CTH 0.50; Hydrotritricum WQ 0.50; D-panthenol 75% 0.20; marine hydrolyzed collagen 0.60; ubiquinone-50 0.012 phenoxyethanol 0.40; perfume q.s.; water to 100.

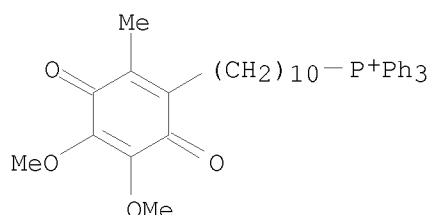
IT 444890-41-9D, Mitoquinone, derivs.

RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)

(hair dyeing method with post-treatment using a bioquinone-containing conditioner)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 5 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:422379 CAPLUS

DOCUMENT NUMBER: 153:453

TITLE: Therapeutic use of coenzyme Q10 and coenzyme Q10-related compounds and formulations

AUTHOR(S): Villalba, Jose M.; Parrado, Cristina; Santos-Gonzalez, Monica; Alcaín, Francisco J.

CORPORATE SOURCE: Edificio Severo Ochoa, Facultad de Ciencias, Departamento de Biología Celular, Fisiología e Inmunología, Universidad de Córdoba, Córdoba, 14014, Spain

SOURCE: Expert Opinion on Investigational Drugs (2010), 19(4), 535-554

CODEN: EOIDER; ISSN: 1354-3784

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Importance of the field: Coenzyme Q10 (CoQ10) is found in blood and in all organs. CoQ10 deficiencies are due to autosomal recessive mutations, aging-related oxidative stress and carcinogenesis processes, and also statin treatment. Many neurodegenerative disorders, diabetes, cancer and muscular and cardiovascular diseases have been associated with low CoQ10 levels, as well as different ataxias and encephalomyopathies. Areas covered in this review: We review the efficacy of a variety of formulations which have been developed to solubilise CoQ10 and promote its better absorption in vivo, and its use in the therapy of pathologies associated with low CoQ10 levels, with emphasis in the results of the clinical trials. Also, we review the use of its analogs idebenone and MitoQ. What the reader will gain: This review covers the most relevant aspects related with the therapeutic use of CoQ10, including existing formulations and their effects on its bioavailability. Take home message: CoQ10 does not cause serious adverse effects in humans and new formulations have been developed that increase CoQ10 absorption. Oral CoQ10 is a viable antioxidant strategy in many diseases, providing a significant to mild symptomatic benefit. Idebenone and MitoQ are promising substitutive CoQ10-related drugs which are well tolerated and safe.

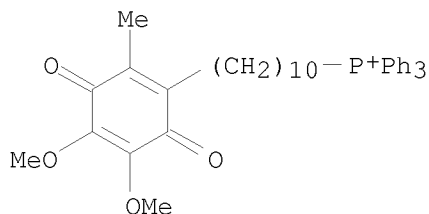
IT 444890-41-9, MitoQ

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic use of coenzyme Q10 and coenzyme Q10-related compds. and formulations for treatment of degenerative diseases)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 211 THERE ARE 211 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L3 ANSWER 6 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:409307 CAPLUS

DOCUMENT NUMBER: 152:422252

TITLE: Compositions and methods for treating viral infections

INVENTOR(S): Sharma, Geeta; Altmeyer, Ralf; Pendharker, Vishal; Chen, Yu; Foley, Michael

PATENT ASSIGNEE(S): Combinatorx Pte. Ltd., Singapore

SOURCE: U.S. Pat. Appl. Publ., 38pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20100081713	A1	20100401	US 2009-406716	20090318
PRIORITY APPLN. INFO.:			US 2008-69917P	P 20080319

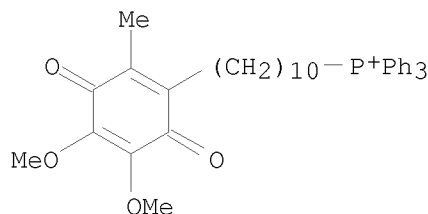
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides compns., methods, and kits for treating or preventing a viral infection (e.g., an infection caused by an influenza virus). A composition comprises a selective serotonin reuptake inhibitor and an addnl. antiviral agent or a pair of agents such as an SSRI and a corticosteroid. Agents and combinations of agents have been identified which reduce inflammatory response in cells infected with an influenza virus, and further, these agents and combinations of agents have been shown to reduce mortality rates of mice infected with an influenza virus. C57/BL6 mice were orally administered treatments starting 4 h before inoculation with LDs of mouse-adapted influenza A virus. The survival rate on day 9 was 0% for vehicle-treated mice. The survival rate of mice receiving sertraline at a dose of 30 mg/kg/day was 22.2% on day 10. Mice treated with a combination of sertraline 30 mg/kg and prednisolone 0.1 mg/kg showed 30% survival on day 10.

IT 444890-41-9, Mitoquinone  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compns. and methods for treating viral infections)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 7 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:151226 CAPLUS

DOCUMENT NUMBER: 152:231278

TITLE: Use of hydrogenated pyrido[4,3-b] indoles for the treatment of oxidative stress

INVENTOR(S): Miller, Guy M.; Wesson, Kieron E.

PATENT ASSIGNEE(S): Edison Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 63pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010014758	A1	20100204	WO 2009-US52163	20090729
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

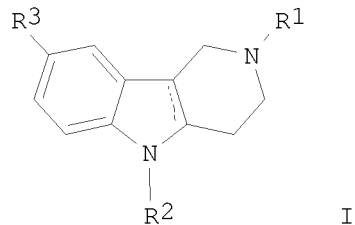
US 20100029706	A1	20100204	US 2009-511934	20090729
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PRIORITY APPLN. INFO.: US 2008-137339P P 20080730

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 152:231278

GI



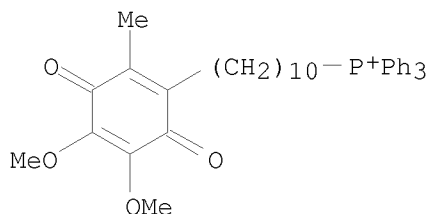
I

AB Methods of treating or suppressing oxidative stress diseases including mitochondrial diseases, impaired energy processing disorders, and diseases of aging such as diabetes and cancer with hydrogenated pyrido[4,3-b]indoles of Formula (I) where the substituents are as in specification, such as dimebolin, are disclosed.

IT 444890-41-9, MitoQ  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(codrug; use of hydrogenated pyrido[4,3-b] indoles for treatment of oxidative stress diseases)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:22080 CAPLUS

DOCUMENT NUMBER: 152:144701

TITLE: Preparation of 2,4,6-trisubstituted pyrido[3,2-d]pyrimidines useful for treating viral infection

INVENTOR(S): Canales, Eda; Chong, Lee S.; Clarke, Michael O'Neil Hanrahan; Lazerwith, Scott E.; Lew, Willard; Liu, Qi; Mitchell, Michael L.; Watkins, William J.; Zhang, Jennifer R.

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 210pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010002998	A1	20100107	WO 2009-US49412	20090701
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV,				

SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,  
IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,  
SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,  
ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2008-78185P

P 20080703

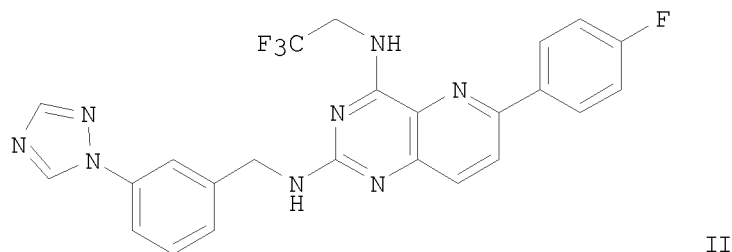
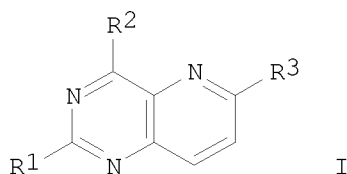
US 2008-84254P

P 20080728

OTHER SOURCE(S):

MARPAT 152:144701

GI

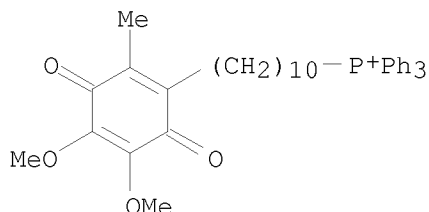


AB The invention relates to pyrido[3,2-d]pyrimidine derivs. represented by the structural formula I: pharmaceutical acceptable addition salts, stereochem. isomeric forms, N-oxides, solvates and pro-drugs thereof, for use in the treatment of hepatitis C. Compds. of formula I wherein R<sup>1</sup> is NHCHR<sup>5</sup>R<sup>6</sup> and NHR<sup>8</sup>; R<sup>2</sup> is NHR<sup>4</sup> and XR<sup>7</sup>; R<sup>3</sup> is (un)substituted alkynyl, (un)substituted Ph, (un)substituted alkenyl, etc.; R<sup>5</sup> and R<sup>8</sup> are independently H, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-10 cycloalkyl, (un)substituted aryl and heterocyclyl; R<sup>7</sup> is (un)substituted C<sub>1</sub>-20 alkyl, C<sub>3</sub>-10 cycloalkyl, aryl, heterocyclyl, etc.; R<sup>8</sup> is C<sub>3</sub>-10 cycloalkyl, (un)substituted heteroaryl and aryl; X is O, S, CH<sub>2</sub>, NH and derivs.; and pharmaceutically acceptable addition salts, stereochem. isomeric forms, N-oxides, solvates and prodrugs thereof, are claimed. Example compound II was prepared by cross-coupling of 3-amino-6-chloropyridine-2-carboxamide with 4-fluorophenylboronic acid; the resulting 3-amino-6-(4-fluorophenyl)pyridine-2-carboxamide underwent cyclization with triphosgene to give 6-(4-fluorophenyl)pyrido[3,2-d]pyrimidine-2,4-diol which underwent chlorination to give 2,4-dichloro-6-(4-fluorophenyl)pyrido[3,2-d]pyrimidine, which underwent double amination with 2,2,2-trifluoroethylamine and 3-(1,3,4-triazol-1-yl)benzylamine to give compound II. All the invention compds. were evaluated for their anti-HCV activity. From the assay, it was determined that compound II exhibited and

EC50

value of < 0.1  $\mu$ M and a CC50 value of < 10  $\mu$ M.

IT 444890-41-9, MitoQ  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (codrug; preparation of trisubstituted pyridopyrimidine compds. useful in  
 treatment of viral infections)  
 RN 444890-41-9 CAPLUS  
 CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
 yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2009:1536376 CAPLUS  
 DOCUMENT NUMBER: 152:55951  
 TITLE: Use of PEGylated type III interferons for the  
 treatment of hepatitis C  
 INVENTOR(S): Hausman, Diana F.; Dodds, Michael G.  
 PATENT ASSIGNEE(S): Zymogenetics, LLC, USA; Bristol-Myers Squibb Co.  
 SOURCE: PCT Int. Appl., 95pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009149377	A1	20091210	WO 2009-US46451	20090605
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2008-59237P	P 20080605
			US 2008-109455P	P 20081029
			US 2009-167763P	P 20090408

AB Methods are disclosed for treating human patients infected with the



hepatitis C virus using pegylated Type III interferons (IL-28A, IL-28B and IL-29) alone or in combination with other antiviral agents.

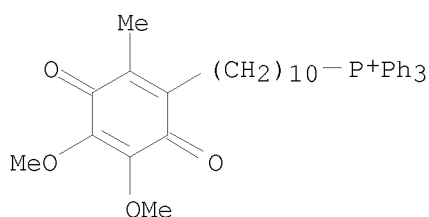
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of PEGylated type III interferons for the treatment of hepatitis C)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1352756 CAPLUS

DOCUMENT NUMBER: 151:568604

TITLE: Mitochondrial-Driven Ubiquinone Enhances Extracellular Calcium-Dependent Nitric Oxide Production and Reduces Glycochenodeoxycholic Acid-Induced Cell Death in Hepatocytes

AUTHOR(S): Gonzalez-Rubio, Sandra; Hidalgo, Ana B.; Ferrin, Gustavo; Bello, Rosario I.; Gonzalez, Raul; Gahete, Manuel D.; Ranchal, Isidora; Rodriguez, Blanca A.; Barrera, Pilar; Aguilar-Melero, Patricia; Linares, Clara I.; Castano, Justo P.; Victor, Victor M.; De la Mata, Manuel; Muntane, Jordi

CORPORATE SOURCE: Liver Research Unit, Reina Sofia University Hospital, Cordoba, Spain

SOURCE: Chemical Research in Toxicology (2009), 22(12), 1984-1991

CODEN: CRTOEC; ISSN: 0893-228X

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ca<sup>2+</sup> mobilization, nitric oxide (NO), and oxidative stress have been involved in cell death induced by hydrophobic bile acid in hepatocytes. The aim of the study was the elucidation of the effect of the antioxidant mitochondrial-driven ubiquinone (Mito Q) on the intracellular Ca<sup>2+</sup> concentration, NO production, and cell death in glycochenodeoxycholic acid (GCDCA)-treated HepG2 cells. The role of the regulation of the intracellular Ca<sup>2+</sup> concentration by Ca<sup>2+</sup> chelators (EGTA or BAPTA-AM), agonist of Ca<sup>2+</sup> entrance (A23187) or NO (L-NAME or NO donor), was assessed during Mito Q cytoprotection in GCDCA-treated HepG2 cells. Cell death, NO synthase (NOS)-1, -2, and -3

expression, Ca<sup>2+</sup> mobilization, and NO production were evaluated. GCDCA reduced the intracellular Ca<sup>2+</sup> concentration and NOS-3 expression and enhanced cell death in HepG2. NO donor prevented and L-NAME enhanced GCDCA-induced cell death. The reduction of Ca<sup>2+</sup> entry by EGTA, but not its release from intracellular stores by BAPTA-AM, reduced the expression of NOS-3 and enhanced cell death in control and GCDCA-treated cells. Mito Q prevented the reduction of intracellular Ca<sup>2+</sup> concentration, NOS-3 expression, NO production, and

cell death in GCDCA-treated HepG2 cells. The conclusion is that the recovery of Ca<sup>2+</sup>-dependent NOS-3 expression by Mito Q may be considered an addnl. cytoprotective property of an antioxidant.

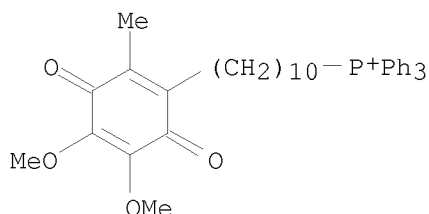
IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antioxidant MitoQ (mitochondrial-driven ubiquinone) enhances extracellular calcium-dependent nitric oxide production and reduces glycochenodeoxycholic acid (GCDCA)-induced cell death in human hepatocytes)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1334557 CAPLUS

DOCUMENT NUMBER: 152:51417

TITLE: MitoQ administration prevents endotoxin-induced cardiac dysfunction

AUTHOR(S): Supinski, G. S.; Murphy, M. P.; Callahan, L. A.

CORPORATE SOURCE: Division of Pulmonary, Critical Care, and Sleep Medicine, University of Kentucky, Lexington, KY, USA  
SOURCE: American Journal of Physiology (2009), 297(4, Pt. 2), R1095-R1102

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sepsis elicits severe alterations in cardiac function, impairing cardiac mitochondrial and pressure-generating capacity. Currently, there are no therapies to prevent sepsis-induced cardiac dysfunction. We tested the hypothesis that administration of a mitochondrially targeted antioxidant, 10-(6'-ubiquinonyl)-decyltriphenylphosphonium (MitoQ), would prevent endotoxin-induced redns. in cardiac mitochondrial and contractile function. Studies were performed on adult rodents (n = 52) given either

saline, endotoxin (8 mg/kg-1/day-1), saline + MitoQ (500  $\mu$ M), or both endotoxin and MitoQ. At 48 h animals were killed and hearts were removed for determination of either cardiac mitochondrial function (using polarog.) or cardiac pressure generation (using the Langendorff technique). We found that endotoxin induced redns. in mitochondrial state 3 respiration rates, the respiratory control ratio, and ATP generation. Moreover, MitoQ administration prevented each of these endotoxin-induced abnormalities,  $P < 0.001$ . We also found that endotoxin produced redns. in cardiac pressure-generating capacity, reducing the systolic pressure-diastolic relation. MitoQ also prevented endotoxin-induced redns. in cardiac pressure generation,  $P < 0.01$ . One potential link between mitochondrial and contractile dysfunction is caspase activation; we found that endotoxin increased cardiac levels of active caspases 9 and 3 ( $P < 0.001$ ), while MitoQ prevented this increase ( $P < 0.01$ ). These data demonstrate that MitoQ is a potent inhibitor of endotoxin-induced mitochondrial and cardiac abnormalities. We speculate that this agent may prove a novel therapy for sepsis-induced cardiac dysfunction.

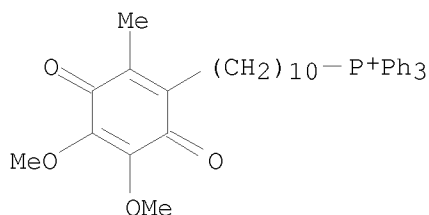
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(MitoQ administration prevents endotoxin-induced cardiac dysfunction)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1266517 CAPLUS

DOCUMENT NUMBER: 151:433935

TITLE: Lipophilic cation-mitochondrially targeted antioxidant compositions for skin care

INVENTOR(S): Murphy, Michael Patrick; Smith, Robin A. J.; Taylor, Kenneth Martin

PATENT ASSIGNEE(S): Antipodean Pharmaceuticals, Inc., N. Z.

SOURCE: U.S. Pat. Appl. Publ., 24 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

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US 20090258841      A1      20091015      US 2009-410318      20090324
WO 2009145982      A1      20091203      WO 2009-US38123      20090324
W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
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    FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
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RW:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
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PRIORITY APPLN. INFO.:

US 2008-41551P

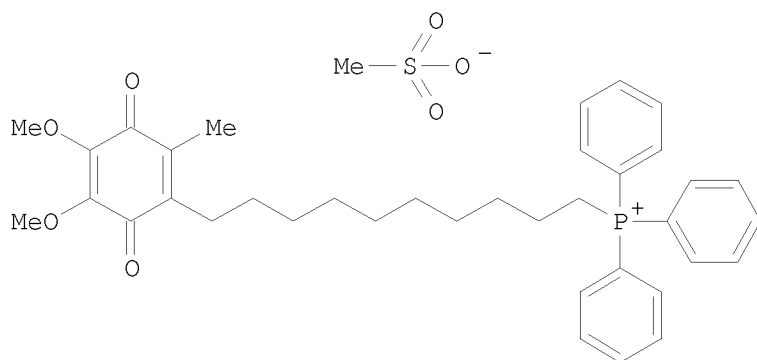
P 20080401

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S):

MARPAT 151:433935

GI



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AB Compns. and methods are disclosed for treating a skin condition that results from reactive oxygen species (ROS) production in skin of a subject, including applying a topical formulation that contains a lipophilic cation-mitochondrially targeted antioxidant compound and that delivers a therapeutically effective amount of the antioxidant compound to skin fibroblasts and keratinocytes. A topical antioxidant formulation is prepared containing MitoQ10 mesylate (I). Examples include I suppression of

ROS

and collagenase production by human skin fibroblast in an in vitro skin aging model.

IT 444890-41-9D, Mitoq, anion salts 845959-50-4  
845959-52-6

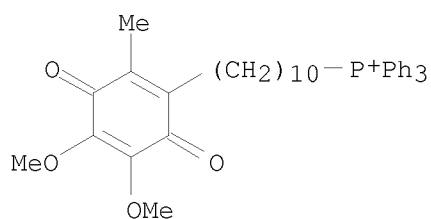
RL: BSU (Biological study, unclassified); COS (Cosmetic use); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)

(lipophilic cation-mitochondrially targeted antioxidant compns. for  
skin care)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-

yl)decyl]triphenyl- (CA INDEX NAME)



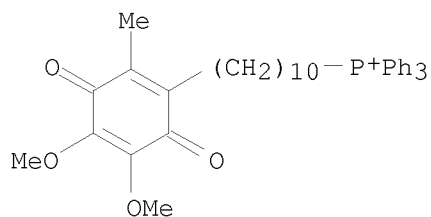
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

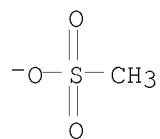
CMF C37 H44 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



RN 845959-52-6 CAPLUS

CN β-Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (1:1) (9CI)  
(CA INDEX NAME)

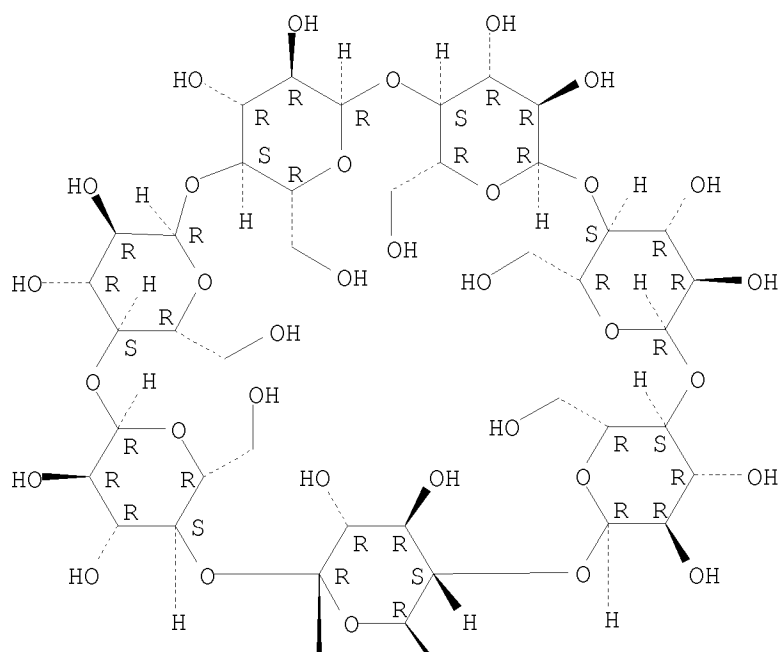
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CRN 7585-39-9

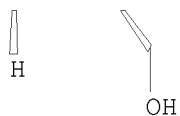
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



CM 2

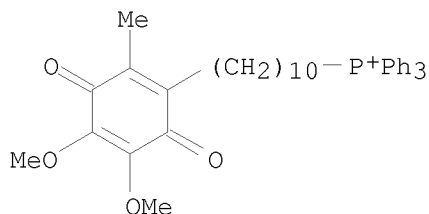
CRN 845959-50-4

CMF C37 H44 O4 P . C H3 O3 S

CM 3

CRN 444890-41-9

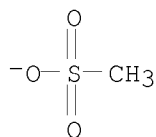
CMF C37 H44 O4 P



CM 4

CRN 16053-58-0

CMF C H3 O3 S



L3 ANSWER 13 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1071258 CAPLUS

DOCUMENT NUMBER: 151:304590

TITLE: The mitochondria-targeted antioxidant MitoQ protects against organ damage in a lipopolysaccharide-peptidoglycan model of sepsis. [Erratum to document cited in CA150:070836]

AUTHOR(S): Lowes, Damon A.; Thottakam, Bensita M. V.; Webster, Nigel R.; Murphy, Michael P.; Galley, Helen F.

CORPORATE SOURCE: Academic Unit of Anaesthesia and Intensive Care, School of Medicine, Institute of Medical Sciences, Foresterhill, Aberdeen, AB25 2ZD, UK

SOURCE: Free Radical Biology & Medicine (2009), 47(7), 1098  
CODEN: FRBMEH; ISSN: 0891-5849

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB On page 1560, in the right column, in paragraph 5, in lines 16-17, "7.5  $\mu\text{mol/kg}$  MitoQ", and "5  $\mu\text{mol/kg/h}$ ", were incorrectly given, and should read: "1.5  $\mu\text{mol/kg}$  MitoQ" and "1  $\mu\text{mol/kg/h}$ ", resp.

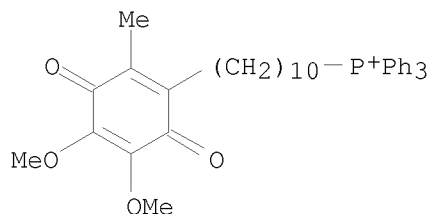
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondria-targeted antioxidant MitoQ protects against organ damage in sepsis model (Erratum))

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 14 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:851191 CAPLUS

DOCUMENT NUMBER: 152:279067

TITLE: Mitochondria-Targeted Antioxidant MitoQ10 Improves Endothelial Function and Attenuates Cardiac Hypertrophy

AUTHOR(S): Graham, Delyth; Huynh, Ngan N.; Hamilton, Carlene A.; Beattie, Elisabeth; Smith, Robin A. J.; Cocheme, Helena M.; Murphy, Michael P.; Dominiczak, Anna F.

CORPORATE SOURCE: British Heart Foundation Glasgow Cardiovascular Research Centre, Faculty of Medicine, University of Glasgow, Glasgow, UK

SOURCE: Hypertension (2009), 54(2), 322-328

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mitochondria are a major site of reactive oxygen species production, which may contribute to the development of cardiovascular disease. Protecting mitochondria from oxidative damage should be an effective therapeutic strategy; however, conventional antioxidants are ineffective, because they cannot penetrate the mitochondria. This study investigated the role of mitochondrial oxidative stress during development of hypertension in the stroke-prone spontaneously hypertensive rat, using the mitochondria-targeted antioxidant, MitoQ10. Eight-week-old male stroke-prone spontaneously hypertensive rats were treated with MitoQ10 (500  $\mu\text{mol/L}$ ;  $n=16$ ), control compound decyltriphenylphosphonium (decylTPP; 500  $\mu\text{mol/L}$ ;  $n=8$ ), or vehicle ( $n=9$ ) in drinking water for 8 wk. Systolic blood pressure was significantly reduced by  $\approx 25$  mm Hg over the 8-wk MitoQ10 treatment period compared with decylTPP ( $F=5.94$ ;  $P=0.029$ ) or untreated controls ( $F=65.6$ ;  $P=0.0001$ ). MitoQ10 treatment significantly improved thoracic aorta NO bioavailability ( $1.16 \pm 0.03$  g/g;  $P=0.002$ , area under the curve) compared with both untreated controls ( $0.68 \pm 0.02$  g/g) and decylTPP-treated rats ( $0.60 \pm 0.06$  g/g). Cardiac hypertrophy was significantly reduced by MitoQ10 treatment compared with untreated control and decylTPP treatment (MitoQ10:  $4.01 \pm 0.05$  mg/g; control:  $4.42 \pm 0.11$  mg/g; and decylTPP:  $4.40 \pm 0.09$  mg/g; ANOVA  $P=0.002$ ). Total MitoQ10 content was measured in liver, heart, carotid artery, and kidney harvested from MitoQ10-treated rats by liquid chromatog.-tandem mass spectrometry. All of the organs analyzed demonstrated detectable levels of MitoQ10, with comparable accumulation in vascular and cardiac tissues. Administration of the mitochondria-targeted antioxidant MitoQ10 protects against the development of hypertension, improves endothelial function, and reduces cardiac hypertrophy in young stroke-prone spontaneously hypertensive rats. MitoQ10 provides a novel



approach to attenuate mitochondrial-specific oxidative damage with the potential to become a new therapeutic intervention in human cardiovascular disease.

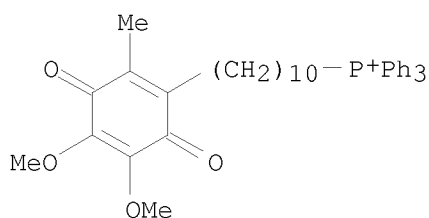
IT 444890-41-9, MitoQ10

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondria-targeted oral MitoQ10 improved endothelial function, reduced cardiac hypertrophy in stroke-prone rat with spontaneous hypertension suggesting its use against mitochondrial oxidative stress in cardiovascular disease patient)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:826004 CAPLUS

DOCUMENT NUMBER: 151:148619

TITLE: Preparation of peptide analogs as inhibitors of cytochrome p450 for improving the pharmacokinetics of codrugs

INVENTOR(S): Desai, Manoj C.; Hui, Hon C.; Liu, Hongtao; Xu, Lianhong

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 132pp.  
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20090175820	A1	20090709	US 2008-340419	20081219
AU 2008346823	A1	20090716	AU 2008-346823	20081219
WO 2009088719	A1	20090716	WO 2008-US87821	20081219

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,

TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,  
 IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,  
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,  
 TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,  
 AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2008-19079P

P 20080104

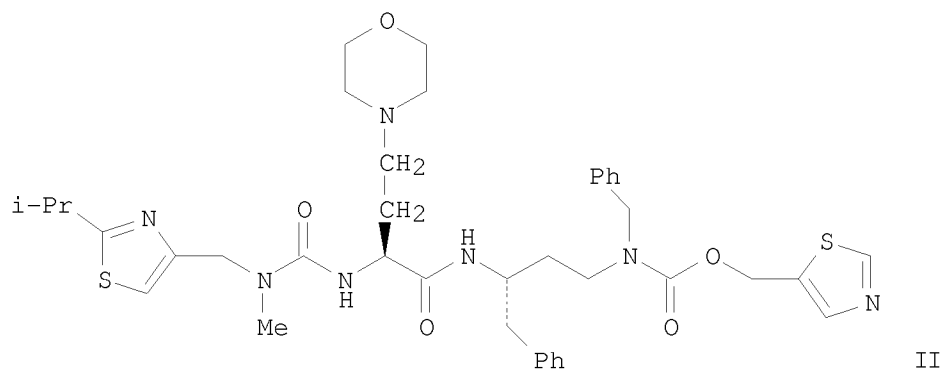
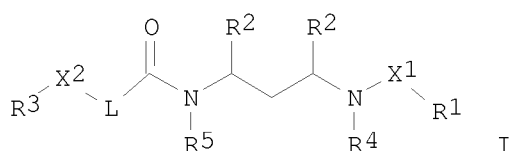
WO 2008-US87821

W 20081219

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 151:148619

GI



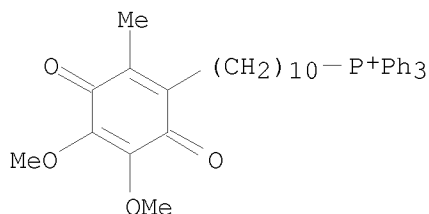
AB The present application provides for a compound of Formula I (wherein X1 is -C(O)-O-, -S(O)-, etc.; X2 is -O-, NH, etc.; L is a covalent bond, alkylene, etc.; R1 is aryl, heteroaryl, etc.; R2 is H, alkyl, etc., R3 is aryl, heteroaryl, etc.; R4 and R5 are independently H, alkyl, etc.) or a pharmaceutically acceptable salt, solvate, and/or ester thereof, compns. containing such compds., therapeutic methods that include the administration of such compds., and therapeutic methods that include the administration of such compds. with at least one addnl. therapeutic agent. I are cytochrome P 450 inhibitors and, as such, can improve the pharmacokinetics of a coadministered drug. I also have a reduced level of protease inhibitory activity and can thus be used to enhance the effectiveness of antiviral drugs while minimizing the potential for eliciting viral resistance. Synthetic procedures for preparing I are exemplified. Example compound II, prepared in a multistep synthesis, had an IC50 between 100 and 200 nM in a CYP450 3A4 inhibition assay.

IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(preparation of peptide analogs as inhibitors of cytochrome P 450 for

improving the pharmacokinetics of codrugs, especially antiviral agents)  
RN 444890-41-9 CAPLUS  
CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 16 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:783818 CAPLUS

DOCUMENT NUMBER: 151:236254

TITLE: Doxorubicin inactivates myocardial cytochrome c oxidase in rats: cardioprotection by Mito-Q

AUTHOR(S): Chandran, Karunakaran; Aggarwal, Deepika; Migrino, Raymond Q.; Joseph, Joy; McAllister, Donna; Konorev, Eugene A.; Antholine, William E.; Zielonka, Jacek; Srinivasan, Satish; Avadhani, Narayan G.; Kalyanaraman, B.

CORPORATE SOURCE: Department of Biophysics and Free Radical Research Center, Medical College of Wisconsin, Milwaukee, WI, USA

SOURCE: Biophysical Journal (2009), 96(4), 1388-1398  
CODEN: BIOJAU; ISSN: 0006-3495

PUBLISHER: Cell Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Doxorubicin (DOX) is used for treating various cancers. Its clin. use is, however, limited by its dose-limiting cardiomyopathy. The exact mechanism of DOX-induced cardiomyopathy still remains unknown. The goals were to investigate the mol. mechanism of DOX-induced cardiomyopathy and cardioprotection by mitoquinone (Mito-Q), a triphenylphosphonium-conjugated analog of coenzyme Q, using a rat model. Rats were treated with DOX, Mito-Q, and DOX plus Mito-Q for 12 wk. The left ventricular function as measured by two-dimensional echocardiog. decreased in DOX-treated rats but was preserved during Mito-Q plus DOX treatment. Using low-temperature ex vivo ESR, a time-dependent decrease in

heme

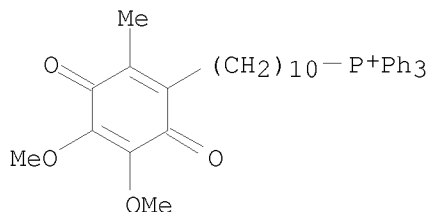
signal was detected in heart tissues isolated from rats administered with a cumulative dose of DOX. DOX attenuated the EPR signals characteristic of the exchange interaction between cytochrome c oxidase (CcO)-Fe(III) heme a<sub>3</sub> and CuB. DOX and Mito-Q together restored these EPR signals and the CcO activity in heart tissues. DOX strongly downregulated the stable expression of the CcO subunits II and Va and had a slight inhibitory effect on CcO subunit I gene expression. Mito-Q restored CcO subunit II and Va expressions in DOX-treated rats. These results suggest a novel cardioprotection mechanism by Mito-Q during DOX-induced cardiomyopathy involving CcO.

IT 444890-41-9, Mito-Q

RL: PAC (Pharmacological activity); BIOL (Biological study)  
(doxorubicin inactivates myocardial cytochrome c oxidase and  
cardioprotection by Mito-Q)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD  
(7 CITINGS)

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:567708 CAPLUS

DOCUMENT NUMBER: 151:191513

TITLE: Pro-oxidant mitochondrial matrix-targeted ubiquinone  
MitoQ10 acts as anti-oxidant at retarded electron  
transport or proton pumping within Complex I

AUTHOR(S): Plecita-Hlavata, Lydie; Jezek, Jan; Jezek, Petr

CORPORATE SOURCE: Department No. 75, Institute of Physiology, Academy of  
Sciences, Prague, 14220, Czech Rep.

SOURCE: International Journal of Biochemistry & Cell Biology  
(2009), 41(8-9), 1697-1707

CODEN: IJBBFU; ISSN: 1357-2725

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oxidative stress of mitochondrial origin, i.e. elevated mitochondrial  
superoxide production, belongs to major factors determining aging and  
oxidative-stress-related diseases. Antioxidants, such as the  
mitochondria-targeted coenzyme Q, MitoQ10, may prevent or cure these  
pathol. conditions. To elucidate pro- and anti-oxidant action of MitoQ10,  
we studied its effects on HepG2 cell respiration, mitochondrial network  
morphol., and rates of superoxide release (above that neutralized by  
superoxide dismutase) to the mitochondrial matrix (Jm). MitoSOX Red  
fluorescence confocal microscopy monitoring of Jm rates showed  
pro-oxidant effects of 3.5-fold increased Jm with MitoQ10. MitoQ10  
induced fission of the mitochondrial network which was recovered after 24  
h. In rotenone-inhibited HepG2 cells (i.e., already under oxidative  
stress) MitoQ10 sharply decreased rotenone-induced Jm, but not together  
with the Complex II inhibitor thenoyltrifluoroacetone. Respiration of  
HepG2 cells and isolated rat liver mitochondria with MitoQ10 increased  
independently of rotenone. The increase was prevented by  
thenoyltrifluoroacetone. These results suggest that MitoQ10 accepts  
electrons prior to the rotenone-bound Q-site, and the Complex II reverse  
mode oxidizes MitoQ10H2 to regenerate MitoQ10. Consequently, MitoQ10 has

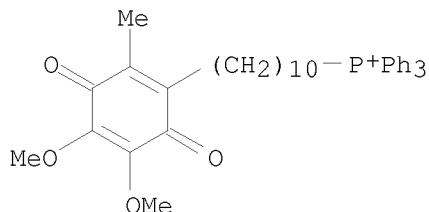
a pro-oxidant role in intact cells, whereas it serves as an antioxidant when Complex I-derived superoxide generation is already elevated due to electron flow retardation. Moreover, unlike mitochondrial uncoupling, MitoQ10 exerted its antioxidant role when Complex I proton pumping was retarded by a hydrophobic amiloride, 5-(N-ethyl-N-isopropyl) amiloride. Consequently, MitoQ10 may be useful in the treatment of diseases originating from impairment of respiratory chain Complex I due to oxidatively damaged mitochondrial DNA, when its targeted delivery to pathogenic tissues is ensured.

IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(Pro-oxidant mitochondrial matrix-targeted ubiquinone MitoQ10 acts as anti-oxidant at retarded electron transport or proton pumping within Complex I)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:523722 CAPLUS

DOCUMENT NUMBER: 150:487794

TITLE: AMPA receptor antagonists for Parkinson's disease and movement disorders

INVENTOR(S): Hanada, Takahisa; Hibi, Shigeki; Miyazaki, Kazuki

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 62pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009054544	A1	20090430	WO 2008-JP69820	20081024
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,				

TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,  
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TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,  
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,  
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2007-996078P

P 20071026

OTHER SOURCE(S): MARPAT 150:487794

AB The invention provides methods for treating Parkinson's disease by administering to patients therapeutically effective amts. of AMPA receptor antagonists in combination with one or more other active ingredients useful for treating Parkinson's disease. The invention provides methods for treating movement disorders by administering to patients therapeutically effective amts. of AMPA receptor antagonists in optionally combination with one or more other active ingredients that are useful for treating movement disorders. The invention also provides pharmaceutical combinations, kits, and pharmaceutical compns. comprising therapeutically effective amts. of AMPA receptor antagonists, and optionally, one or more other active ingredients that are useful for treating Parkinson's disease and/or movement disorders.

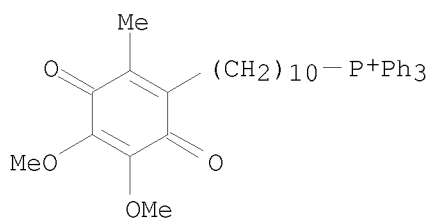
IT 444890-41-9, Mitoquinone

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AMPA receptor antagonists for Parkinson's disease and movement disorders)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:397447 CAPLUS

DOCUMENT NUMBER: 151:259809

TITLE: The mitochondria targeted antioxidant MitoQ protects against fluoroquinolone-induced oxidative stress and mitochondrial membrane damage in human Achilles tendon cells

AUTHOR(S): Lowes, Damon A.; Wallace, Carol; Murphy, Michael P.; Webster, Nigel R.; Galley, Helen F.

CORPORATE SOURCE: Division of Applied Medicine, School of Medicine & Dentistry, University of Aberdeen, Aberdeen, AB41 8TJ, UK

SOURCE: Free Radical Research (2009), 43(4), 323-328  
CODEN: FRARER; ISSN: 1071-5762

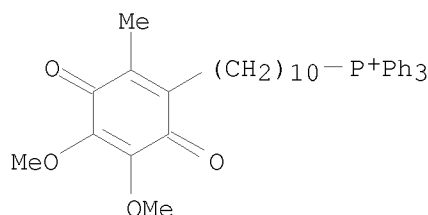
PUBLISHER: Informa Healthcare  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Tendinitis and tendon rupture during treatment with fluoroquinolone antibiotics is thought to be mediated via oxidative stress. This study investigated whether ciprofloxacin and moxifloxacin cause oxidative stress and mitochondrial damage in cultured normal human Achilles' tendon cells and whether an antioxidant targeted to mitochondria (MitoQ) would protect against such damage better than a non-mitochondria targeted antioxidant. Human tendon cells from normal Achilles' tendons were exposed to 0-0.3 mM antibiotic for 24 h and 7 days in the presence of 1  $\mu$ M MitoQ or an untargeted form, idebenone. Both moxifloxacin and ciprofloxacin resulted in  $\leq$  a 3-fold increase in the rate of oxidation of dichlorodihydrofluorescein, a marker of general oxidative stress in tenocytes and loss of mitochondrial membrane permeability. In cells treated with MitoQ the oxidative stress was less and mitochondrial membrane potential was maintained. Mitochondrial damage to tenocytes during fluoroquinolone treatment may be involved in tendinitis and tendon rupture.

IT 444890-41-9, MitoQ  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(antioxidant MitoQ protects against fluoroquinolone-induced oxidative stress in human Achilles tendon cells)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:209919 CAPLUS

DOCUMENT NUMBER: 150:297730

TITLE: Transport and metabolism of some cationic ubiquinone antioxidants (MitoQn) in Caco-2 cell monolayers

AUTHOR(S): Li, Yan; Fawcett, J. Paul; Zhang, Hu; Tucker, Ian G.  
CORPORATE SOURCE: School of Pharmacy, University of Otago, Dunedin, N. Z.

SOURCE: European Journal of Drug Metabolism and Pharmacokinetics (2008), 33(4), 199-204  
CODEN: EJDPD2; ISSN: 0378-7966

PUBLISHER: Medecine et Hygiene

DOCUMENT TYPE: Journal

LANGUAGE: English

AB MitoQn are mitochondria-targeted antioxidants with structures linking a

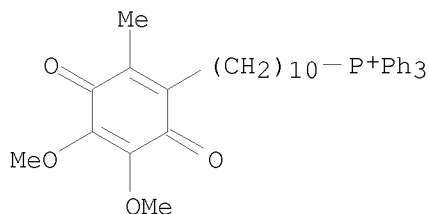
triphenylphosphonium cation to an ubiquinone moiety by a linear n-carbon alkyl chain. The antioxidant efficacy of MitoQn has been shown to be optimum when n = 10 but little is known about the relative transport and metabolism of these homologs. The present study examined the absorptive and secretory transport and metabolism of MitoQn (n = 3, 5 and 10) in Caco-2 cell monolayers. During absorptive transport in the apical-to-basolateral (AB) direction, intracellular accumulation was proportional to lipophilicity but permeation (PappAB) was not, being high for MitoQ3 and low for MitoQ5 and MitoQ10. Secretory transport was greater than absorptive transport with efflux ratios (PappBA/PappAB) for n = 3, 5 and 10 of 2.3, 24.9 and 4.0, resp. In the presence of the P-glycoprotein inhibitor cyclosporine A (CsA) 30  $\mu$ M, PappAB values for n = 3, 5 and 10 were increased by 12, 195% and 30%, resp. whereas PappBA values were decreased by 81%, 61% and 68% resp. In the presence of protein (4% bovine serum albumin) on the B side, PappAB of MitoQ10 (log P 3.44) increased 9-fold whereas PappAB of MitoQ5 (log P 1.14) remained unchanged, both with no change in permeability to the paracellular probe, mannitol. During transport, metabolism to the corresponding reduced ubiquinol species and their sulfate and glucuronide conjugates was detected by liquid chromatog. tandem mass spectrometry. In conclusion, the permeation of these cationic ubiquinone antioxidants in Caco-2 cell monolayers depends on a balance between lipophilicity, transporter affinity, protein binding and affinity for phase 2 metabolizing enzymes.

IT 845959-50-4D, monosulfates and monoglucuronide conjugates  
845959-57-1D, monosulfates and monoglucuronide conjugates  
954111-83-2D, monosulfates and monoglucuronide conjugates  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(transport and metabolism of cationic ubiquinone antioxidants)  
RN 845959-50-4 CAPLUS  
CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

CMF C37 H44 O4 P

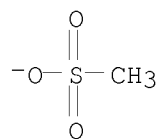


CM 2

CRN 16053-58-0

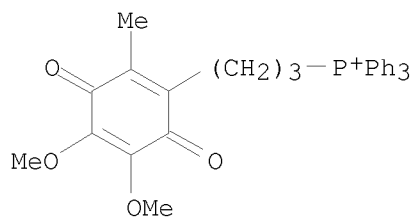
CMF C H3 O3 S





RN 845959-57-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



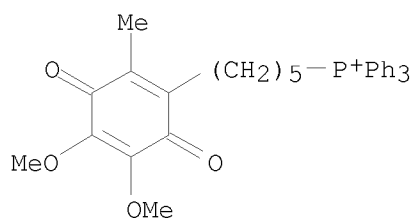
RN 954111-83-2 CAPLUS

CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 794485-94-2

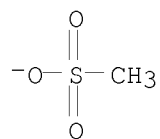
CMF C32 H34 O4 P



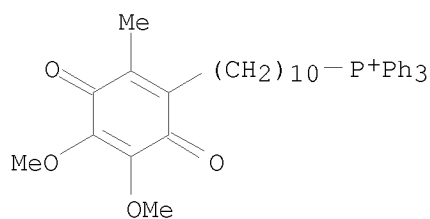
CM 2

CRN 16053-58-0

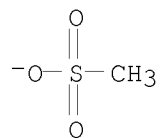
CMF C H3 O3 S



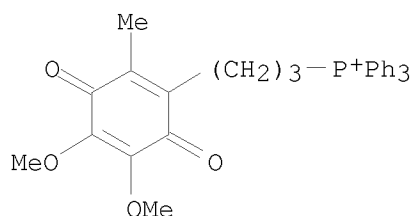
IT 845959-50-4 845959-57-1 954111-83-2  
 RL: PKT (Pharmacokinetics); BIOL (Biological study)  
 (transport and metabolism of cationic ubiquinone antioxidants)  
 RN 845959-50-4 CAPLUS  
 CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)  
 CM 1  
 CRN 444890-41-9  
 CMF C37 H44 O4 P



CM 2  
 CRN 16053-58-0  
 CMF C H3 O3 S



RN 845959-57-1 CAPLUS  
 CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



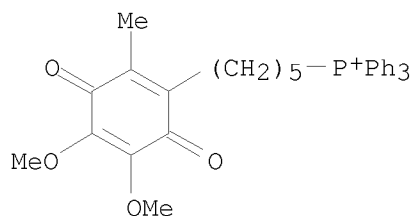
RN 954111-83-2 CAPLUS

CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 794485-94-2

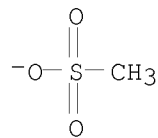
CMF C32 H34 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

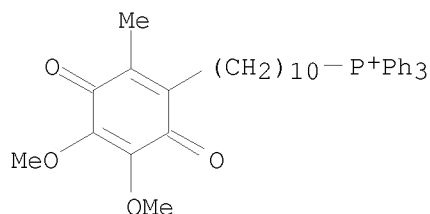
L3 ANSWER 21 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:177695 CAPLUS

DOCUMENT NUMBER: 151:308952

TITLE: Collagen fragmentation promotes oxidative stress and elevates matrix metalloproteinase-1 in fibroblasts in

aged human skin  
AUTHOR(S): Fisher, Gary J.; Quan, Taihao; Purohit, Trupta; Shao, Yuan; Cho, Moon Kyun; He, Tianyuan; Varani, James; Kang, Sewon; Voorhees, John J.  
CORPORATE SOURCE: Department of Dermatology, Medical School, University of Michigan, Ann Arbor, MI, USA  
SOURCE: American Journal of Pathology (2009), 174(1), 101-114  
CODEN: AJPA44; ISSN: 0002-9440  
PUBLISHER: American Society for Investigative Pathology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Aged human skin is fragile because of fragmentation and loss of type I collagen fibrils, which confer strength and resiliency. We report here that dermal fibroblasts express increased levels of collagen-degrading matrix metalloproteinases-1 (MMP-1) in aged (>80 years old) compared with young (21 to 30 years old) human skin in vivo. Transcription factor AP-1 and  $\alpha 2\beta 1$  integrin, which are key regulators of MMP-1 expression, are also elevated in fibroblasts in aged human skin in vivo. MMP-1 treatment of young skin in organ culture causes fragmentation of collagen fibrils and reduces fibroblast stretch, consistent with reduced mech. tension, as observed in aged human skin. Limited fragmentation of three-dimensional collagen lattices with exogenous MMP-1 also reduces fibroblast stretch and mech. tension. Furthermore, fibroblasts cultured in fragmented collagen lattices express elevated levels of MMP-1, AP-1, and  $\alpha 2\beta 1$  integrin. Importantly, culture in fragmented collagen raises intracellular oxidant levels and treatment with antioxidant MitoQ10 significantly reduces MMP-1 expression. These data identify pos. feedback regulation that couples age-dependent MMP-1-catalyzed collagen fragmentation and oxidative stress. We propose that this self-perpetuating cycle promotes human skin aging. These data extend the current understanding of the oxidative theory of aging beyond a cellular-centric view to include extracellular matrix and the critical role that connective tissue microenvironment plays in the biol. of aging.  
IT 444890-41-9, Mitoquinone  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (aged human skin in vivo and young collagen lattice cell culture model show collagen fragmentation alter fibroblast shape, mech. tension, integrin expression and elevate oxidative stress, matrix metalloproteinase-1 gene expression)  
RN 444890-41-9 CAPLUS  
CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)  
REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:170709 CAPLUS

DOCUMENT NUMBER: 151:92990

TITLE: Targeting antioxidants to mitochondria by conjugation to lipophilic cations

AUTHOR(S): Murphy, Michael P.

CORPORATE SOURCE: MRC Dunn Human Nutrition Unit, Wellcome Trust, Cambridge, UK

SOURCE: Drug-Induced Mitochondrial Dysfunction (2008), 575-587. Editor(s): Dykens, James A.; Will, Yvonne. John Wiley &amp; Sons, Inc.: Hoboken, N. J. CODEN: 69LIVZ; ISBN: 978-0-470-11131-4

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review on the background and work to date on mitochondria-targeted antioxidants. Topics covered include reactive oxygen species (ROS) and drug design, MitoQ and MitoE, potential toxicity, bioavailability, approaches, and pharmaceutical development of MitoQ10.

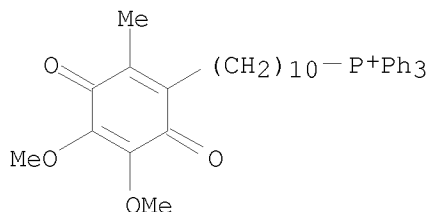
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(targeting antioxidant MitoQ10 to mitochondria by conjugation to lipophilic triphenylphosphonium cation may be beneficial in treatment of patient with ischemia-reperfusion injury, liver damage, Parkinson's disease or type II diabetes)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:159417 CAPLUS

DOCUMENT NUMBER: 150:187603

TITLE: Mitochondrial targeted coenzyme Q, superoxide, and fuel selectivity in endothelial cells

AUTHOR(S): Fink, Brian D.; O'Malley, Yunxia; Dake, Brian L.; Ross, Nicolette C.; Prisinzano, Thomas E.; Sivitz, William I.

CORPORATE SOURCE: Division of Endocrinology and Metabolism, Department of Internal Medicine, Iowa City Veterans Affairs Medical Center and the University of Iowa, Iowa City, IA, USA

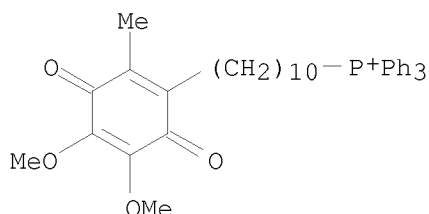
SOURCE: PLoS One (2009), 4(1), No pp. given  
CODEN: POLNCL; ISSN: 1932-6203  
URL: <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0004250>  
PUBLISHER: Public Library of Science  
DOCUMENT TYPE: Journal; (online computer file)  
LANGUAGE: English

AB Previously, we reported that the "antioxidant" compound "mitoQ" (mitochondrial-targeted ubiquinol/ubiquinone) actually increased superoxide production by bovine aortic endothelial (BAE) cell mitochondria incubated with complex I but not complex II substrates. To further define the site of action of the targeted coenzyme Q compound, we extended these studies to include different substrate and inhibitor conditions. In addition, we assessed the effects of mitoquinone on mitochondrial respiration, measured respiration and mitochondrial membrane potential in intact cells, and tested the intriguing hypothesis that mitoquinone might impart fuel selectivity in intact BAE cells. In mitochondria respiring on differing concns. of complex I substrates, mitoquinone and rotenone had interactive effects on ROS consistent with redox cycling at multiple sites within complex I. Mitoquinone increased respiration in isolated mitochondria respiring on complex I but not complex II substrates. Mitoquinone also increased oxygen consumption by intact BAE cells. Moreover, when added to intact cells at 50 to 1000 nM, mitoquinone increased glucose oxidation and reduced fat oxidation, at doses that did not alter membrane potential or induce cell toxicity. Although high dose mitoquinone reduced mitochondrial membrane potential, the pos. charged mitochondrial-targeted cation, decyltriphenylphosphonium (mitoquinone without the coenzyme Q moiety), decreased membrane potential more than mitoquinone, but did not alter fuel selectivity. Therefore, non-specific effects of the pos. charge were not responsible and the quinone moiety is required for altered nutrient selectivity. In summary, the interactive effects of mitoquinone and rotenone are consistent with redox cycling at more than one site within complex I. In addition, mitoquinone has substrate dependent effects on mitochondrial respiration, increases respiration by intact cells, and alters fuel selectivity favoring glucose over fatty acid oxidation at the intact cell level.

IT 444890-41-9, MitoQ  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)  
(interactive effects of mitochondrial targeted coenzyme Q and rotenone are consistent with redox cycling at more than one site within complex I in endothelial cells)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:143000 CAPLUS

DOCUMENT NUMBER: 151:69361

TITLE: Mitochondrial approaches for neuroprotection

AUTHOR(S): Chaturvedi, Rajnish K.; Beal, M. Flint

CORPORATE SOURCE: Department of Neurology and Neuroscience, Weill Medical College, Cornell University, New York, NY, USA

SOURCE: Annals of the New York Academy of Sciences (2008), 1147(Mitochondria and Oxidative Stress in Neurodegenerative Disorders), 395-412  
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. A large body of evidence from postmortem brain tissue and genetic anal. in humans and biochem. and pathol. studies in animal models (transgenic and toxin) of neurodegeneration suggest that mitochondrial dysfunction is a common pathol. mechanism. Mitochondrial dysfunction from oxidative stress, mitochondrial DNA deletions, pathol. mutations, altered mitochondrial morphol., and interaction of pathogenic proteins with mitochondria leads to neuronal demise. Therefore, therapeutic approaches targeting mitochondrial dysfunction and oxidative damage hold great promise in neurodegenerative diseases. This review discusses the potential therapeutic efficacy of creatine, coenzyme Q10, idebenone, synthetic triterpenoids, and mitochondrial targeted antioxidants (MitoQ) and peptides (SS-31) in in vitro studies and in animal models of Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Alzheimer's disease. We have also reviewed the current status of clin. trials of creatine, coenzyme Q10, idebenone, and MitoQ in neurodegenerative disorders. Further, we discuss newly identified therapeutic targets, including peroxisome proliferator-activated receptor- $\gamma$ -coactivator and sirtuins, which provide promise for future therapeutic developments in neurodegenerative disorders.

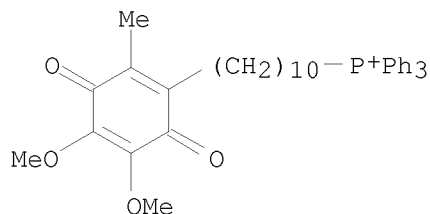
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondrial targeted antioxidant MitoQ showed neuroprotective effect and reduced mitochondrial dysfunction in patient with neurodegenerative disease)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 37 THERE ARE 37 CAPLUS RECORDS THAT CITE THIS RECORD (37 CITINGS)  
REFERENCE COUNT: 200 THERE ARE 200 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:142988 CAPLUS

DOCUMENT NUMBER: 152:138177

TITLE: The mitochondrial antioxidants MitoE2 and MitoQ10 increase mitochondrial  $\text{Ca}^{2+}$  load upon cell stimulation by inhibiting  $\text{Ca}^{2+}$  efflux from the organelle

AUTHOR(S): Leo, Sara; Szabadkai, Gyorgy; Rizzuto, Rosario

CORPORATE SOURCE: Department of Experimental and Diagnostic Medicine, Section of General Pathology, Interdisciplinary Center for the Study of Inflammation and Emilia Romagna Laboratory for Genomics and Biotechnology, University of Ferrara, Ferrara, Italy

SOURCE: Annals of the New York Academy of Sciences (2008), 1147(Mitochondria and Oxidative Stress in Neurodegenerative Disorders), 264-274  
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mitochondrial reactive oxygen species (ROS) production is recognized as a major pathogenic event in a number of human diseases, and mitochondrial scavenging of ROS appears a promising therapeutic approach. Recently, two mitochondrial antioxidants have been developed; conjugating  $\alpha$ -tocopherol and the ubiquinol moiety of coenzyme Q to the lipophilic triphenylphosphonium cation ( $\text{TPP}^+$ ), denominated MitoE2 and MitoQ10, resp. We have investigated the effect of these compds. on mitochondrial  $\text{Ca}^{2+}$  homeostasis, which controls processes as diverse as activation of mitochondrial dehydrogenases and pro-apoptotic morphol. changes of the organelle. We demonstrate that treatment of HeLa cells with both MitoE2 and MitoQ10 induces (albeit with different efficacy) a major enhancement of the increase in matrix  $\text{Ca}^{2+}$  concentration triggered by cell

stimulation with the inositol 1,4,5-triphosphate-generating agonist histamine. The effect is a result of the inhibition of  $\text{Ca}^{2+}$  efflux from the organelle and depends on the  $\text{TPP}^+$  moiety of these compds. Overall, the data identify an effect independent of their antioxidant activity, that on the one hand may be useful in addressing disorders in which mitochondrial  $\text{Ca}^{2+}$  handling is impaired (e.g., mitochondrial diseases) and on the other may favor mitochondrial  $\text{Ca}^{2+}$  overload and thus increase cell sensitivity to apoptosis (thus possibly counteracting the benefits of the antioxidant activity).

IT 444890-41-9, MitoQ

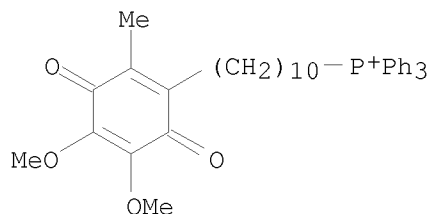
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondrial antioxidants MitoE2 and MitoQ10 increase mitochondrial  $\text{Ca}^{2+}$  load upon cell stimulation by inhibiting mitochondrial  $\text{Ca}^{2+}$  efflux)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)





OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)  
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:142976 CAPLUS

DOCUMENT NUMBER: 151:69358

TITLE: Mitochondria-targeted antioxidants in the treatment of diasease

AUTHOR(S): Smith, Robin A. J.; Adlam, Victoria J.; Blaikie, Frances H.; Manas, Abdul-Rahman B.; Porteous, Carolyn M.; James, Andrew M.; Ross, Meredith F.; Logan, Angela; Cocheme, Helena M.; Trnka, Jan; Prime, Tracy A.; Abakumova, Irina; Jones, Bruce A.; Filipovska, Aleksandra; Murphy, Michael P.

CORPORATE SOURCE: Department of Chemistry, University of Otago, Dunedin, N. Z.

SOURCE: Annals of the New York Academy of Sciences (2008), 1147(Mitochondria and Oxidative Stress in Neurodegenerative Disorders), 105-111  
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Mitochondrial oxidative damage is thought to contribute to a wide range of human diseases; therefore, the development of approaches to decrease this damage may have therapeutic potential. Mitochondria-targeted antioxidants that selectively block mitochondrial oxidative damage and prevent some types of cell death have been developed. These compds. contain antioxidant moieties, such as ubiquinone, tocopherol, or nitroxide, that are targeted to mitochondria by covalent attachment to a lipophilic triphenylphosphonium cation. Because of the large mitochondrial membrane potential, the cations are accumulated within the mitochondria inside cells. There, the conjugated antioxidant moiety protects mitochondria from oxidative damage. Here, we outline some of the work done to date on these compds. and how they may be developed as therapies.

IT 444890-41-9, MitoQ

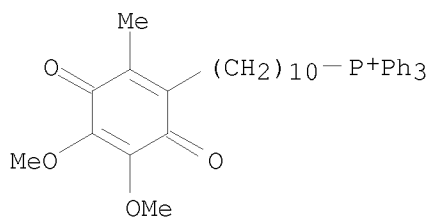
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antioxidant MitoQ prevents targeted mitochondria from oxidative damage and could be effective in treating patient with ischemia-reperfusion injury, steatohepatitis and chronic neurodegenerative diseases)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-

yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)  
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:39840 CAPLUS

DOCUMENT NUMBER: 150:463311

TITLE: Mitochondria-targeted plastoquinone derivatives as tools to interrupt execution of the aging program. 1. Cationic plastoquinone derivatives: Synthesis and in vitro studies

AUTHOR(S): Antonenko, Y. N.; Avetisyan, A. V.; Bakeeva, L. E.; Chernyak, B. V.; Chertkov, V. A.; Domnina, L. V.; Ivanova, O. Yu.; Izyumov, D. S.; Khailova, L. S.; Klishin, S. S.; Korshunova, G. A.; Lyamzaev, K. G.; Muntyan, M. S.; Nepryakhina, O. K.; Pashkovskaya, A. A.; Pletjushkina, O. Yu.; Pustovidko, A. V.; Roginsky, V. A.; Rokitskaya, T. I.; Ruuge, E. K.; Saprunova, V. B.; Severina, I. I.; Simonyan, R. A.; Skulachev, I. V.; Skulachev, M. V.; Sumbatyan, N. V.; Sviryaeva, I. V.; Tashlitsky, V. N.; Vassiliev, J. M.; Vyssokikh, M. Yu.; Yaguzhinsky, L. S.; Zamyatnin, A. A., Jr.; Skulachev, V. P.

CORPORATE SOURCE: Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University, Moscow, 119991, Russia

SOURCE: Biochemistry (Moscow) (2008), 73(12), 1273-1287

CODEN: BIORAK; ISSN: 0006-2979

PUBLISHER: Pleiades Publishing, Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Synthesis of cationic plastoquinone derivs. (SkQs) containing pos. charged phosphonium or rhodamine moieties connected to plastoquinone by decane or pentane linkers is described. It is shown that SkQs (i) easily penetrate through planar, mitochondrial, and outer cell membranes, (ii) at low (nanomolar) concns., posses strong antioxidant activity in aqueous solution,

BLM, lipid micelles, liposomes, isolated mitochondria, and cells, (iii) at higher (micromolar) concns., show pronounced prooxidant activity, the "window" between anti- and prooxidant concns. being very much larger than for MitoQ, a cationic ubiquinone derivative showing very much lower antioxidant activity and higher prooxidant activity, (iv) are reduced by the respiratory chain to SkQH2, the rate of oxidation of SkQH2 being lower

than the rate of SkQ reduction, and (v) prevent oxidation of mitochondrial cardiolipin by  $\text{OH}\cdot$ . In HeLa cells and human fibroblasts, SkQs operate as powerful inhibitors of the ROS-induced apoptosis and necrosis. For the two most active SkQs, namely SkQ1 and SkQR1,  $\text{CI}/2$  values for inhibition of the  $\text{H}_2\text{O}_2$ -induced apoptosis in fibroblasts appear to be as low as  $1 + 10^{-11}$  and  $8 + 10^{-13}$  M, resp. SkQR1, a fluorescent representative of the SkQ family, specifically stains a single type of organelles in the living cell, i.e. energized mitochondria. Such specificity is explained by the fact that it is the mitochondrial matrix that is the only neg.-charged compartment inside the cell. Assuming that the  $\Delta\psi$  values on the outer cell and inner mitochondrial membranes are about 60 and 180 mV, resp., and taking into account distribution coefficient of SkQ1 between lipid and water (about 13,000:1), the SkQ1 concentration in the inner leaflet of the inner mitochondrial membrane should be  $1.3 + 10^8$  times higher than in the extracellular space. This explains the very high efficiency of such compds. in expts. on cell cultures. It is concluded that SkQs are rechargeable, mitochondria-targeted antioxidants of very high efficiency and specificity. Therefore, they might be used to effectively prevent ROS-induced oxidation of lipids and proteins in the inner mitochondrial membrane in vivo.

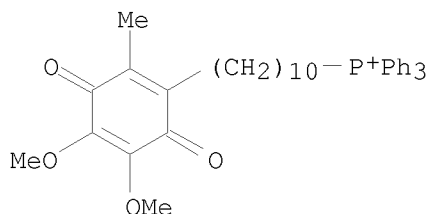
IT 444890-41-9P, MitoQ

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(mitochondria-targeted plastoquinone derivs. as tools to interrupt execution of aging program and cationic plastoquinone derivs. and synthesis and in vitro studies)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)  
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 28 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:20361 CAPLUS

DOCUMENT NUMBER: 150:98048

TITLE: Preparation of purine derivatives as modulators of toll-like receptor 7

INVENTOR(S): Graupe, Michael; Halcomb, Randall L.

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 169pp.

CODEN: PIXXD2

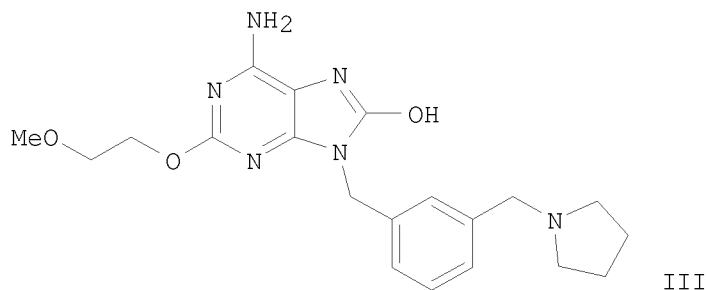
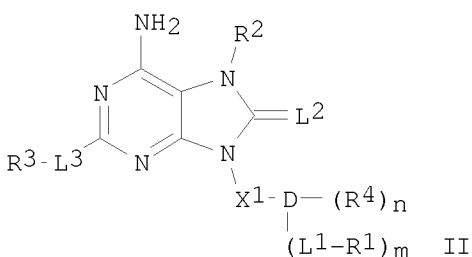
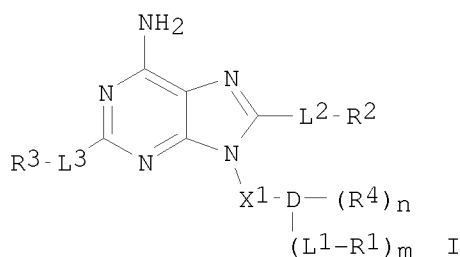
DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009005687	A1	20090108	WO 2008-US7955	20080626
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2008271127	A1	20090108	AU 2008-271127	20080626
CA 2691444	A1	20090108	CA 2008-2691444	20080626
US 20090047249	A1	20090219	US 2008-215598	20080626
AR 67182	A1	20090930	AR 2008-102756	20080626
EP 2170888	A1	20100407	EP 2008-779791	20080626
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
KR 2010039368	A	20100415	KR 2010-702075	20080626
MX 2009013832	A	20100310	MX 2009-13832	20091216
IN 2009DN08396	A	20100716	IN 2009-DN8396	20091222
CN 101784548	A	20100721	CN 2008-80104326	20100225
PRIORITY APPLN. INFO.:			US 2007-937726P	P 20070629
			US 2007-959714P	P 20070716
			WO 2008-US7955	W 20080626

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 150:98048; MARPAT 150:98048

GI



AB Purine derivs. of formulas I or II [X1 = NH, O, alkylene, etc.; D = (hetero)cycllyl, etc.; L1 = alkylene; L2, L3 = bond, NH, O, S; etc.; R1 = NR5R6; R2 = H, halo, alkyl, cycloalkyl, acyl, etc.; R3 = alkyl, cycloalkyl, etc.; R4 = halo, CN, N3, NO2, alkyl, OH, NH2, etc.; R4, R5 = H, alkyl, etc.; R4R5 = alkylene, etc.; m = 1-2; n = 0-5] are prepared as modulators of toll-like receptor 7. The compds. can be used in combination therapy of diseases. Thus, III was prepared, and had ECmax value < 5 nM in human peripheral blood mononuclear cell assay.

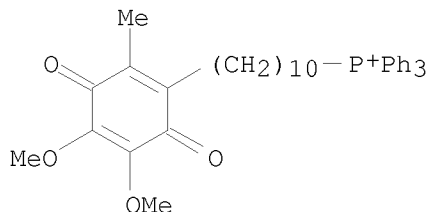
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(purine derivs. as TLR7 modulators useful in combination therapy of diseases)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1525375 CAPLUS

DOCUMENT NUMBER: 150:324155  
TITLE: Reactivity of ubiquinone and ubiquinol with superoxide and the hydroperoxyl radical: implications for in vivo antioxidant activity  
AUTHOR(S): Maroz, Andrej; Anderson, Robert F.; Smith, Robin A. J.; Murphy, Michael P.  
CORPORATE SOURCE: Department of Chemistry, The University of Auckland, Auckland, 1142, N. Z.  
SOURCE: Free Radical Biology & Medicine (2009), 46(1), 105-109  
CODEN: FRBMEH; ISSN: 0891-5849  
PUBLISHER: Elsevier B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

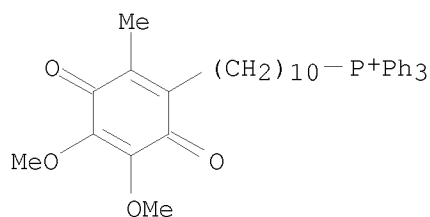
AB Endogenous ubiquinones (UQ) such as coenzyme Q10 are essential electron carriers in the mitochondrial respiratory chain, and the reduced ubiquinol form (UQH2) is a chain-breaking antioxidant, decreasing oxidative damage caused by lipid peroxidn. within mitochondria. Consequently, exogenous UQ are used as therapies to decrease mitochondrial oxidative damage. The proximal radical produced during mitochondrial oxidative stress is superoxide ( $O\cdot-2$ ) and the reaction between UQ and  $O\cdot-2$  to form the ubisemiquinone radical anion ( $UQ\cdot-$ ) may also be important for the scavenging of  $O\cdot-2$  by exogenous UQ. The situation in vivo is that many UQ are predominantly located in the hydrophobic membrane core, from which  $O\cdot-2$  will be excluded but its conjugate acid,  $HOO\cdot$ , can enter. The reactivity of UQ or UQH2 with  $HOO\cdot$  has not been reported previously. Here a pulse radiolysis study on the reactions between UQ/UQH2 and  $O\cdot-2/HOO\cdot$  in water and in solvent systems mimicking the surface and core of biol. membranes has been undertaken.  $O\cdot-2$  reacts very rapidly with UQ, suggesting that this may contribute to the scavenging of  $O\cdot-2$  in vivo. In contrast, UQH2 reacts relatively slowly with  $HOO\cdot$ , but rapidly with other oxygen- and carbon-centered radicals, indicating that the antioxidant role of UQH2 is mainly in preventing lipid peroxidn.

IT 444890-41-9, Mitoquinone

RL: BSU (Biological study, unclassified); BIOL (Biological study) (reactivity of ubiquinone and ubiquinol with superoxide and the hydroperoxyl radical and the implications for in vivo antioxidant activity)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1403634 CAPLUS

DOCUMENT NUMBER: 150:70836

TITLE: The mitochondria-targeted antioxidant MitoQ protects against organ damage in a

AUTHOR(S): lipopolysaccharide-peptidoglycan model of sepsis  
Lowe, Damon A.; Thottakam, Bensita M. V.; Webster, Nigel R.; Murphy, Michael P.; Galley, Helen F.

CORPORATE SOURCE: Academic Unit of Anaesthesia and Intensive Care, School of Medicine, Institute of Medical Sciences, University of Aberdeen, Aberdeen, AB25 2ZD, UK

SOURCE: Free Radical Biology &amp; Medicine (2008), 45(11), 1559-1565

CODEN: FRBMEH; ISSN: 0891-5849

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sepsis is characterized by a systemic dysregulated inflammatory response and oxidative stress, often leading to organ failure and death. Development of organ dysfunction associated with sepsis is now accepted to be due at least in part to oxidative damage to mitochondria. MitoQ is an antioxidant selectively targeted to mitochondria that protects mitochondria from oxidative damage and which was shown to decrease mitochondrial damage in animal models of oxidative stress. We hypothesised that if oxidative damage to mitochondria does play a significant role in sepsis-induced organ failure, then MitoQ should modulate inflammatory responses, reduce mitochondrial oxidative damage, and thereby ameliorate organ damage. To assess this, we investigated the effects of MitoQ in vitro in an endothelial cell model of sepsis and in vivo in a rat model of sepsis. In vitro MitoQ decreased oxidative stress and protected mitochondria from damage as indicated by a lower rate of reactive oxygen species formation and by maintenance of the mitochondrial membrane potential. MitoQ also suppressed proinflammatory cytokine release from the cells while the production of the anti-inflammatory cytokine interleukin-10 was increased by MitoQ. In a lipopolysaccharide-peptidoglycan rat model of the organ dysfunction that occurs during sepsis, MitoQ treatment resulted in lower levels of biochemical markers of acute liver and renal dysfunction, and mitochondrial membrane potential was augmented in most organs. These findings suggest that the use of mitochondria-targeted antioxidants such as MitoQ may be beneficial in sepsis.

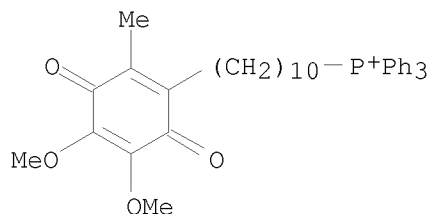
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondria-targeted antioxidant MitoQ protects against organ damage in sepsis model)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS  
RECORD (18 CITINGS)  
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 31 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2008:1339809 CAPLUS  
DOCUMENT NUMBER: 149:525491  
TITLE: Mitochondrially target antioxidants  
INVENTOR(S): Murphy, Michael P.; Smith, Robin A.J.  
PATENT ASSIGNEE(S): Antipodean Pharmaceuticals, Inc., USA  
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S.  
Ser. No. 799,779.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080275005	A1	20081106	US 2008-109170	20080424
WO 9926954	A1	19990603	WO 1998-NZ173	19981125
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
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US 6331532	B1	20011218	US 2000-577877	20000525
US 20020052342	A1	20020502	US 2001-968838	20011003
US 20030069208	A1	20030410	US 2002-272914	20021018
NZ 547101	A	20090731	NZ 2003-547101	20030822
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US 20040106579	A1	20040603	US 2003-722542	20031128
WO 2005019232	A1	20050303	WO 2004-NZ196	20040823
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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 SN, TD, TG

WO 2005019233 A1 20050303 WO 2004-NZ197 20040823  
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 SN, TD, TG  
 US 20050245487 A1 20051103 US 2005-172916 20050705  
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 US 20080161267 A1 20080703 US 2006-568655 20060831  
 US 20070238709 A1 20071011 US 2007-568654 20070222  
 US 20070270381 A1 20071122 US 2007-799779 20070502

PRIORITY APPLN. INFO.:

WO 1998-NZ173 A2 19981125  
 US 2000-577877 A1 20000525  
 US 2001-968838 B1 20011003  
 US 2002-272914 B1 20021018  
 NZ 2003-527800 A 20030822  
 NZ 2003-529153 A 20031023  
 US 2003-722542 B1 20031128  
 NZ 2004-533555 A 20040614  
 NZ 2004-533556 A 20040614  
 WO 2004-NZ196 W 20040823  
 WO 2004-NZ197 W 20040823  
 US 2005-172916 A1 20050705  
 US 2006-568655 A2 20060831  
 US 2007-568654 A2 20070222  
 US 2007-799779 A2 20070502  
 NZ 1997-329255 A 19971125

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides mitochondrially targeted antioxidant compds. A compound of the invention comprises a lipophilic cation covalently coupled to an antioxidant moiety. In preferred embodiments, the lipophilic cation is the tri-Ph phosphonium cation, and the compound is P+(Ph3)XR.Z- where X=linking group, Z=anion, and R=antioxidant moiety. Also provided are pharmaceutical compns. containing the mitochondrially targeted antioxidant compds., and methods of therapy or prophylaxis of patients who would benefit from reduced oxidative stress, which comprise the step of administering the compds. of the invention. Mitoquinol was prepared and was tested in spontaneously hypertensive rats and was found to possess significant antihypertensive activity.

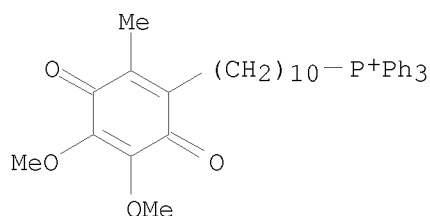
IT 336184-91-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(mitochondrially targeted antioxidants)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



IT 845959-50-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(mitochondrially targeted antioxidants)

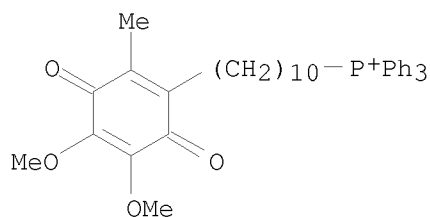
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

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CRN 444890-41-9

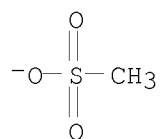
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CM 2

CRN 16053-58-0

CMF C H3 O3 S

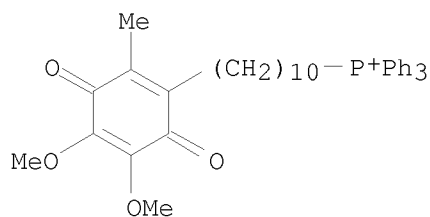


IT 336184-92-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(mitochondrially targeted antioxidants)

RN 336184-92-0 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1), labeled with tritium (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

L3 ANSWER 32 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1289139 CAPLUS

DOCUMENT NUMBER: 150:508532

TITLE: Kinetic Analysis of Permeation of Mitochondria-Targeted Antioxidants Across Bilayer Lipid Membranes

AUTHOR(S): Rokitskaya, Tatyana I.; Klishin, Sergey S.; Severina, Inna I.; Skulachev, Vladimir P.; Antonenko, Yuri N.

CORPORATE SOURCE: A. N. Belozersky Institute of Physico-Chemical Biology, Moscow State University, Moscow, 119992, Russia

SOURCE: Journal of Membrane Biology (2008), 224(1-3), 9-19  
CODEN: JMBBBO; ISSN: 0022-2631

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

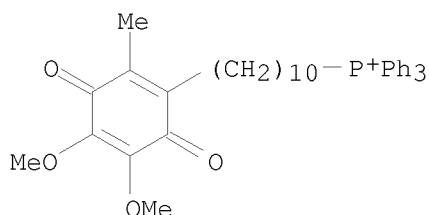
AB Mitochondria-targeted antioxidants consisting of a quinone part conjugated with a lipophilic cation via a hydrocarbon linker were previously shown to prevent oxidative damage to mitochondria in vitro and in vivo. In the present work, we studied the permeation of a series of compds. of this type across a planar bilayer phospholipid membrane. For this purpose, relaxation of the elec. current after a voltage jump was measured. With respect to the characteristic time of the relaxation process reflecting the permeation rate, hydrophobic cations can be ranked in the following series: 10(plastoquinonyl) decylrhodamine 19 (SkQR1) >10-(6'-plastoquinonyl) decyltriphenylphosphonium (SkQ1) >10-(6'-methylplastoquinonyl) decyltriphenylphosphonium (SkQ3) >10-(6'-ubiquinonyl) decyltriphenylphosphonium (MitoQ). Thus, the permeation rate increased with (1) an increase in the size of the hydrophobic cation and (2) an increase in hydrophobicity of the quinone moiety. SkQ1 containing plastoquinone was shown to be more permeable through the membrane compared to MitoQ containing ubiquinone, which might be the reason for more pronounced beneficial action of SkQ1 in vitro and in vivo. The above approach can be recommended for the search for new antioxidants or other compds. targeted to mitochondria.

IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)  
(kinetic anal. of permeation of mitochondria-targeted antioxidants across bilayer lipid membranes)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 33 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1288933 CAPLUS

DOCUMENT NUMBER: 149:526871

TITLE: Cations SkQ1 and MitoQ accumulated in mitochondria delay opening of ascorbate/FeSO<sub>4</sub>-induced nonspecific pore in the inner mitochondrial membrane

AUTHOR(S): Khailova, L. S.; Dedukhova, V. I.; Mokhova, E. N.

CORPORATE SOURCE: Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University, Moscow, 119992, Russia

SOURCE: Biochemistry (Moscow) (2008), 73(10), 1121-1124

CODEN: BIORAK; ISSN: 0006-2979

PUBLISHER: Pleiades Publishing, Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is known that an addition of FeSO<sub>4</sub> in the presence of ascorbic acid to cells or mitochondria can injure energy coupling and some other functions in mitochondria. The present study demonstrates that decrease in ascorbate concentration from 4 to 0.2 mM in the presence of the same low concns.

of FeSO<sub>4</sub> accelerates the nonspecific pore opening, while cyclosporin A prevents and under some conditions reverses the pore opening. Hydrophobic cations SkQ1 and MitoQ (structural analogs of plastoquinone and coenzyme Q10, resp.) delay pore opening, SkQ1 being more efficient. It is known that an increase in matrix ADP concentration delays pore opening, while an addition

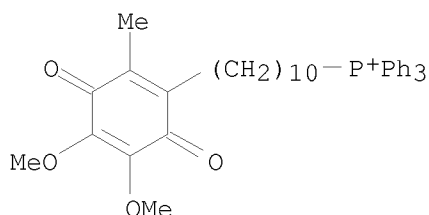
of carboxyatractylate to mitochondria accelerates the beginning of pore opening. Preliminary addition of SkQ1 into a mitochondrial suspension increased the effect of ADP and decreased the effect of carboxyatractylate. These results suggest that under the conditions used SkQ1 protects mitochondria from oxidative damage as an antioxidant when added at extremely low concns.

IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CoQ analog; cations SkQ1 and MitoQ accumulated in mitochondria delay  
opening of ascorbate/FeSO4-induced nonspecific pore in inner  
mitochondrial membrane)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 34 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1245991 CAPLUS

DOCUMENT NUMBER: 150:345197

TITLE: Neonatal rat hypoxia-ischemia: effect of the anti-oxidant mitoquinol, and S-PBN

AUTHOR(S): Hobbs, Catherine E.; Murphy, Michael P.; Smith, Robin A. J.; Oorschot, Dorothy E.

CORPORATE SOURCE: Departments of Anatomy and Structural Biology, University of Otago, Dunedin, N. Z.

SOURCE: Pediatrics International (Richmond, Australia) (2008), 50(4), 481-488

CODEN: JAMMFW; ISSN: 1328-8067

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The production of oxygen free radicals after perinatal hypoxia-ischemia is thought to play a critical role in the pathogenesis of the brain injury. Administration of anti-oxidants may thus be neuroprotective. The aim of the present study was to investigate the effect of a mitochondria-targeted anti-oxidant mitoquinol (mitoQ) administered in the form of the prodrug mitoquinone, and an extracellular anti-oxidant N-tert-butyl-(2-sulfophenyl)-nitron (S-PBN; Aldrich, St Louis, MO, USA), on neuronal survival in the rat striatum after acute perinatal hypoxia-ischemia. Mitoquinone at 17  $\mu\text{mol/L}$  ( $n = 6$ ) or 51  $\mu\text{mol/L}$  ( $n = 6$ ), or its diluent ( $n = 12$ ), was continuously infused over 3 days into the right striatum of Sprague-Dawley rats. Infusion was via an Alzet micro-osmotic pump (Alza, Los Angeles, CA, USA), stereotactically implanted on postnatal day (PN) 7 under anesthesia. In another experiment, S-PBN (100 mg/kg) ( $n = 8$ ) or its diluent ( $n = 8$ ) was administered in six s.c. injections every 12 h from the evening of PN7. Hypoxia-ischemia was induced on PN8 by right common carotid artery ligation under anesthesia, followed 2.5 h later by exposure to 8% oxygen for 1.5 h. On PN14 the pups were euthanized and 40  $\mu\text{m}$  serial sections were cut through the entire striatum. The total number of medium-spiny neurons within the right striatum was stereol. determined using the optical disector/Cavalieri method. No

significant difference was seen in the total number of striatal medium-spiny neurons between the 17  $\mu\text{mol/L}$  or 51  $\mu\text{mol/L}$  mitoQ-treated pups and their resp. diluent-treated controls. No significant difference was seen in the total number of striatal medium-spiny neurons between the S-PBN-treated and diluent-treated pups. Solely targeting mitochondrial oxidants with mitoQ, or extracellular oxidants with S-PBN, is not protective for striatal medium-spiny neurons after perinatal hypoxia-ischemia.

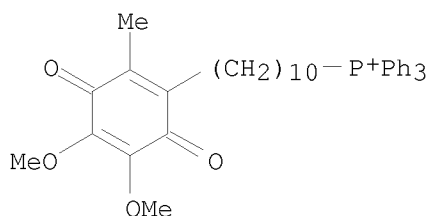
IT 336184-91-9, Mitoquinone bromide

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondria-targeted antioxidant mitoquinol administered in form of prodrug mitoquinone bromide showed no protective effect for medium-spiny neuron survival in rat striatum after acute perinatal hypoxia-ischemia)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



● Br<sup>-</sup>

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 35 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1113947 CAPLUS

DOCUMENT NUMBER: 152:389535

TITLE: Estimation of the lipophilicity of some antioxidants of new generation

AUTHOR(S): Matyushin, A. A.; Tsarev, D. A.; Grigorenko, M. A.; Fedorov, I. I.; Ramenskaya, G. V.; Tashlitskii, V. N.; Skulachev, V. P.

CORPORATE SOURCE: A. N. Belozersky Institute of Physico-Chemical Biology, Russia

SOURCE: Farmatsiya (Moscow, Russian Federation) (2008), (5), 23-29

CODEN: FRMTAL; ISSN: 0367-3014

PUBLISHER: Izdatel'skii Dom "Russkii Vrach"

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB To exactly estimate the lipophilicity of new antioxidants that selectively accumulate in the mitochondria (MitoQ and SkQ1), their log P values were

determined using four different methods. The classical "shake-flask" method (n-octanol/water distribution), as well as computing modeling showed an excellent coincidence for the log P values. On the contrary, the methods based on chromatog. parameters (retention time and retention factor) were unacceptable for these compds. The log P value obtained for SkQ1 (4.11 units) was within the optimum lipophilicity required for penetration through different cellular membranes.

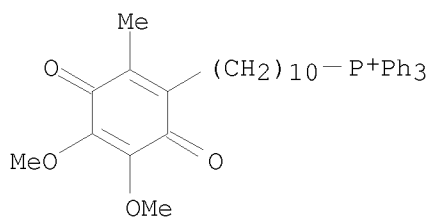
IT 444890-41-9, MitoQ

RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(estimation of the lipophilicity of some antioxidants of new generation)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 36 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1045198 CAPLUS

DOCUMENT NUMBER: 149:308144

TITLE: Preparation of peptidomimetics as modulators of pharmacokinetic properties of therapeutics by inhibiting cytochrome P450 monooxygenase

INVENTOR(S): Desai, Manoj C.; Hong, Allen Y.; Hui, Hon C.; Liu, Hongtao; Vivian, Radall W.; Xu, Lianhong

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 432pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

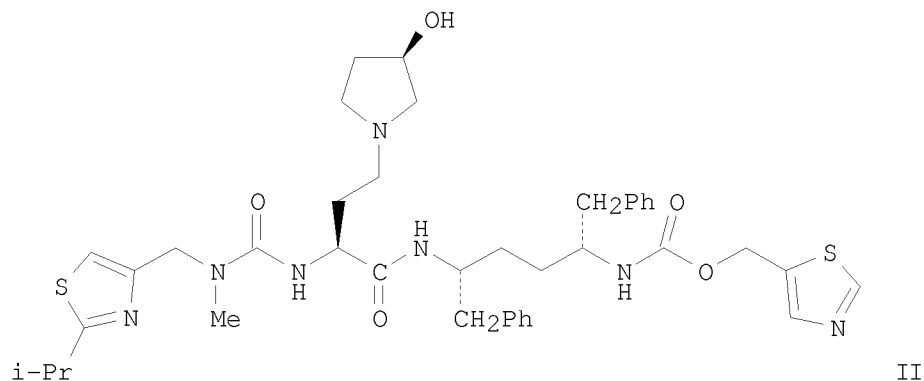
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WO 2008103949	A1	20080828	WO 2008-US54788	20080222
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AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2008218186	A1	20080828	AU 2008-218186	20080222
CA 2678907	A1	20080828	CA 2008-2678907	20080222
US 20080207620	A1	20080828	US 2008-36124	20080222
AR 65439	A1	20090610	AR 2008-100737	20080222
EP 2118082	A1	20091118	EP 2008-743531	20080222
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KR 2009122261	A	20091126	KR 2009-719921	20080222
JP 2010519314	T	20100603	JP 2009-551044	20080222
AU 2008275744	A1	20090115	AU 2008-275744	20080703
CA 2692331	A1	20090115	CA 2008-2692331	20080703
WO 2009008989	A1	20090115	WO 2008-US8231	20080703
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US 20090181902	A1	20090716	US 2008-217496	20080703
AR 67412	A1	20091007	AR 2008-102884	20080703
EP 2170851	A1	20100407	EP 2008-826245	20080703
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KR 2010040896	A	20100421	KR 2010-702076	20080703
IN 2009DN05324	A	20100423	IN 2009-DN5324	20090819
MX 2009008935	A	20091102	MX 2009-8935	20090820
CN 101679325	A	20100324	CN 2008-80013255	20091023
MX 2009013960	A	20100217	MX 2009-13960	20091217
IN 2009DN08537	A	20100723	IN 2009-DN8537	20091229
CN 101796040	A	20100804	CN 2008-80105422	20100303
US 20100189687	A1	20100729	US 2010-528185	20100407
PRIORITY APPLN. INFO.:				
			US 2007-903228P	P 20070223
			US 2007-958716P	P 20070706
			WO 2008-US54788	W 20080222
			WO 2008-US8231	W 20080703
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT				
OTHER SOURCE(S): MARPAT 149:308144				
GI				



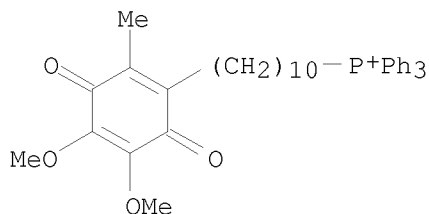


AB The invention is related to the preparation of R8YG3COG2(R1)G1(R2)CONR3CH(L3A)CH2CH2CH(L3A)NR5COOXR9 [I; L3 = independently at each occurrence (un)substituted alkylene; A = independently at each occurrence (un)substituted aryl; X = heterocyclalkyl; Y = heterocyclalkyl, alkyl; G1, G2 = independently CH, N, with the proviso that G1 and G2 are different; G3 = NR7, O; R1, R3, R5, R7 = independently H, (un)substituted aryl/alkyl; R2 = amino/hydroxy/alkoxy/alkyl, NHCONH2 and derivs., etc.; R8, R9 are each one or more substituents selected from H, halo, CN, (un)substituted alkyl], their pharmaceutically acceptable salts, solvates and esters, and compns. containing them which improve the pharmacokinetics of a co-administered drug which is metabolized by cytochrome P 450 monooxygenase. Thus, a multi-step synthesis starting from N-methyl-N-[[2-(1-methylethyl)-4-thiazolyl]methyl]-N'-[(3S)-tetrahydro-2-oxo-3-furanyl]urea (preparation given) was given for II. I inhibited CYP450 3A4 (IC50 = 100-4700 nM), CYP450 2C9 (IC50 = 100-10,000 nM) and protease (EC50 = 140-30,000 nM in an anti HIV-1 cell culture assay). I alone or in combination with one or more addnl. therapeutic agents which are metabolized by cytochrome P 450 monooxygenase are useful for treating a viral infection, e.g. HIV (no data).

IT 444890-41-9, MitoQ  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compds. as modulators of pharmacokinetic properties of therapeutic agents useful in combination therapy of diseases)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)  
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 37 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:787495 CAPLUS

DOCUMENT NUMBER: 149:261445

TITLE: Protective effects of mitochondria-targeted  
antioxidant SkQ in aqueous and lipid membrane  
environments

AUTHOR(S): Antonenko, Y. N.; Roginsky, V. A.; Pashkovskaya, A.  
A.; Rokitskaya, T. I.; Kotova, E. A.; Zaspas, A. A.;  
Chernyak, B. V.; Skulachev, V. P.

CORPORATE SOURCE: A. N. Belozersky Institute of Physico-Chemical  
Biology, Moscow State University, Moscow, 119991,  
Russia

SOURCE: Journal of Membrane Biology (2008), 222(3), 141-149  
CODEN: JMBBBO; ISSN: 0022-2631

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antioxidant activity of mitochondria-targeted small mols., SkQ1 and  
MitoQ (conjugates of a lipophilic decyltriphenylphosphonium cation with an  
antioxidant moiety of a plastoquinone and ubiquinone, resp.), was studied  
in aqueous solution and in a lipid environment, i.e., micelles, liposomes, and  
planar bilayer lipid membranes. Reactive oxygen species (ROS) were  
generated by azo initiators or Fe<sup>2+</sup> with or without  
tert-butyl-hydroperoxide. Chemiluminescence, fluorescence, O<sub>2</sub>  
consumption, and inactivation of gramicidin peptide channels were measured  
to detect antioxidant activity. In all of the systems studied, SkQ1 was  
shown to effectively scavenge ROS. The scavenging was inherent to the  
reduced form of the quinone (SkQ1H<sub>2</sub>). In the majority of the above model  
systems, SkQ1 exhibited higher antioxidant activity than MitoQ. It is  
concluded that SkQ1H<sub>2</sub> operates as a ROS scavenger in both aqueous and lipid  
environments, being effective at preventing ROS-induced damage to membrane  
lipids as well as membrane-embedded peptides.

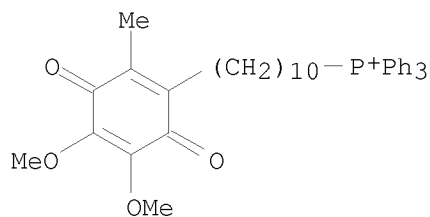
IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(protective effects of mitochondria-targeted antioxidant SkQ in aqueous and  
lipid membrane environments)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS

RECORD (12 CITINGS)  
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

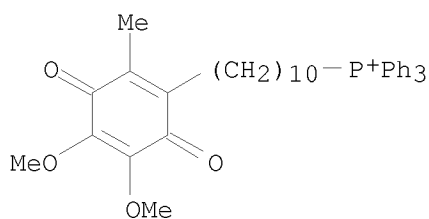
L3 ANSWER 38 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2008:754464 CAPLUS  
DOCUMENT NUMBER: 149:238503  
TITLE: Targeting lipophilic cations to mitochondria  
AUTHOR(S): Murphy, Michael P.  
CORPORATE SOURCE: MRC Dunn Human Nutrition Unit, Wellcome Trust,  
Cambridge, CB2 0XY, UK  
SOURCE: Biochimica et Biophysica Acta, Bioenergetics (2008),  
1777(7-8), 1028-1031  
CODEN: BBBEB4; ISSN: 0005-2728  
PUBLISHER: Elsevier Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. Mitochondrial function and dysfunction contributes to a range  
of important aspects of biomedical research. Consequently there is  
considerable interest in developing approaches to modify and report on  
mitochondria in cells and in vivo. One approach has been to target  
bioactive mols. to mitochondria by conjugating them to lipophilic cations.  
Due to the large mitochondrial membrane potential, the cations are  
accumulated within mitochondria inside cells. This approach had been used  
to develop mitochondria-targeted antioxidants that selectively block  
mitochondrial oxidative damage and prevent some types of cell death and  
also to develop probes of mitochondrial function. Here we outline some of  
the background to the development of these compds.

IT 444890-41-9, MitoQ  
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological  
study); USES (Uses)  
(targeting lipophilic cations to mitochondria)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS  
RECORD (28 CITINGS)  
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 39 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2008:459952 CAPLUS  
DOCUMENT NUMBER: 149:47117  
TITLE: Rapid and extensive uptake and activation of  
hydrophobic triphenylphosphonium cations within cells

AUTHOR(S): Ross, Meredith F.; Prime, Tracy A.; Abakumova, Irina; James, Andrew M.; Porteous, Carolyn M.; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: Wellcome Trust/MRC Building, Medical Research Council Dunn Human Nutrition Unit, Cambridge, CB2 0XY, UK

SOURCE: Biochemical Journal (2008), 411(3), 633-645

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

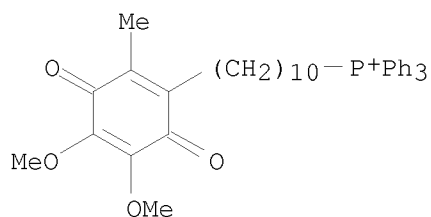
AB Mitochondria-targeted mols. comprising the lipophilic TPP (triphenylphosphonium) cation covalently linked to a hydrophobic bioactive moiety are used to modify and probe mitochondria in cells and in vivo. However, it is unclear how hydrophobicity affects the rate and extent of their uptake into mitochondria within cells, making it difficult to interpret expts. because their intracellular concentration in different compartments is uncertain. To address this issue, we compared the uptake into both isolated mitochondria and mitochondria within cells of two hydrophobic TPP derivs., [3H]MitoQ (mitoquinone) and [3H]DecylTPP, with the more hydrophilic TPP cation [3H]TPMP (methyltriphenylphosphonium). Uptake of MitoQ by mitochondria and cells was described by the Nernst equation and was .apprx.5-fold greater than that for TPMP, as a result of its greater binding within the mitochondrial matrix. DecylTPP was also taken up extensively by cells, indicating that increased hydrophobicity enhanced uptake. Both MitoQ and DecylTPP were taken up very rapidly into cells, reaching a steady state within 15 min, compared with .apprx.8 h for TPMP. This far faster uptake was the result of the increased rate of passage of hydrophobic TPP mols. through the plasma membrane. Within cells MitoQ was predominantly located within mitochondria, where it was rapidly reduced to the ubiquinol form, consistent with its protective effects in cells and in vivo being due to the ubiquinol antioxidant. The strong influence of hydrophobicity on TPP cation uptake into mitochondria within cells facilitates the rational design of mitochondria-targeted compds. to report on and modify mitochondrial function in vivo.

IT 444890-41-9, Mitoquinone

RL: BSU (Biological study, unclassified); BIOL (Biological study) (rapid and extensive uptake and activation of hydrophobic triphenylphosphonium cations within cells)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 40 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2008:352859 CAPLUS  
 DOCUMENT NUMBER: 148:394354  
 TITLE: Compositions and methods for treatment of viral diseases  
 INVENTOR(S): Johansen, Lisa M.; Owens, Christopher M.; Mawhinney, Christina; Chappell, Todd W.; Brown, Alexander T.; Frank, Michael G.; Altmeyer, Ralf  
 PATENT ASSIGNEE(S): Combinatorx (Singapore) Pre. Ltd., Singapore  
 SOURCE: PCT Int. Appl., 237pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033466	A2	20080320	WO 2007-US19932	20070913
WO 2008033466	A3	20081211		
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US 20080161324	A1	20080703	US 2007-900893	20070913
AR 62794	A1	20081203	AR 2007-104083	20070914
PRIORITY APPLN. INFO.:			US 2006-844463P	P 20060914
			US 2006-874061P	P 20061211

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Based on the results of the authors screen identifying compds. and combinations of compds. having antiviral activity, the present invention features compns., methods, and kits useful in the treatment of viral diseases. In certain embodiments, the viral disease is caused by a single stranded RNA virus, a flaviviridae virus, or a hepatic virus. In particular embodiments, the viral disease is viral hepatitis (e.g., hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E). Also featured are screening methods for identification of novel compds. that may be used to treat a viral disease.

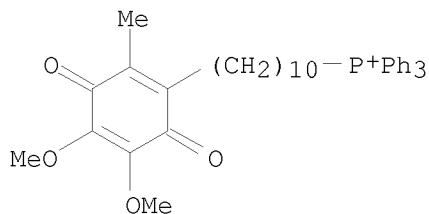
IT 845959-50-4, Mitoquinone  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compns. and methods for treatment of viral diseases)

RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

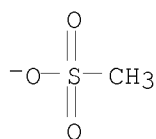
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CM 2

CRN 16053-58-0  
CMF C H3 O3 S



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD  
(3 CITINGS)

L3 ANSWER 41 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2008:199007 CAPLUS  
DOCUMENT NUMBER: 149:26511  
TITLE: Interactions of positively charged ubiquinone analog  
(MitoQ10) with DT-diaphorase in liver mitochondria  
AUTHOR(S): Kargin, V. I.; Motovilov, K. A.; Vysokikh, M. Yu.;  
Yaguzhinskii, L. S.  
CORPORATE SOURCE: A. N. Belozerskii Scientific-Research Institute of  
Physico-Chemical Biology, M. V. Lomonosov Moscow State  
University, Moscow, 119991, Russia  
SOURCE: Biologicheskie Membrany (2008), 25(1), 34-40  
CODEN: BIMEE9; ISSN: 0233-4755  
PUBLISHER: Izdatel'stvo Nauka  
DOCUMENT TYPE: Journal  
LANGUAGE: Russian

AB MitoQ - a pos. charged analog of CoQ - has been studied as an electron transport cofactor in liver mitochondria. NADH-dependent DT-diaphorase is able to reduce MitoQ at a high rate. MitoQH2 in the presence of malate can restore an electron flow from NADH to oxygen blocked by rotenone. Respiration restored by MitoQ is blocked by dicumarol, mixothiazol, and antimycin A. Therefore, in the presence of MitoQ the following electron transport chain is operating in mitochondria: NADH → DT-diaphorase → MitoQ → complex III → complex IV → oxygen. It is shown also that MitoQH2 in the presence of malate (but not succinate) reduces oxygen in the o-center of mitochondrial bcl-complex giving superoxide anion. This reactive oxygen species induces opening of

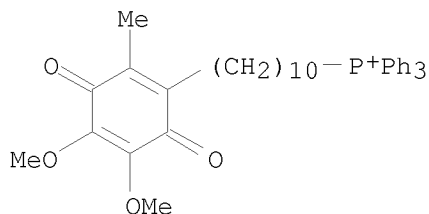
non-specific pore, which leads to the block of oxidative phosphorylation. The data obtained allow considering MitoQ as an analog of hydrophilic quinones, such as duroquinone and K3, which are well-known substrates of DT-diaphorase, but not as an analog of a natural ubiquinone.

IT 444890-41-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(vinteractions of pos. charged ubiquinone analog (MitoQ10) with  
DT-diaphorase in liver mitochondria)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L3 ANSWER 42 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:164099 CAPLUS

DOCUMENT NUMBER: 148:206611

TITLE: Methods for reducing anthracycline-induced toxicity

INVENTOR(S): Kalyanaraman, Balaraman; Kalivendi, Shasi Vardhan;  
Joseph, Joy

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 21pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080032940	A1	20080207	US 2007-834799	20070807
PRIORITY APPLN. INFO.:			US 2006-836247P	P 20060807

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods for treating cancers/tumors include administering to a subject an effective amount of a mitochondria-targeted antioxidant alone or in combination with a chemotherapeutic agents. Likewise, methods for mitigating toxicity associated with a chemotherapeutic agent include administering an effective amount of a mitochondria-targeted antioxidant with a single or with multiple chemotherapeutic agents. The invention relates more particularly to coadministering a mitochondria-targeted antioxidant with a chemotherapeutic agent to attenuate the agent's toxicity to normal cells and to enhance its toxicity to tumor cells. At low micromolar concns., mitochondria-targeted antioxidant MitoQ differentially affected normal cells and tumor cells. MitoQ synerized with doxorubicin (DOX) to enhance caspase-3 activity in tumor cell lines

(MCF-7, MCF-10A and SH-SY5Y), but not in normal cells lines (CM and 1-19c2). In fact, MitoQ attenuated DOX-induced caspase-3 activity in normal cell lines.

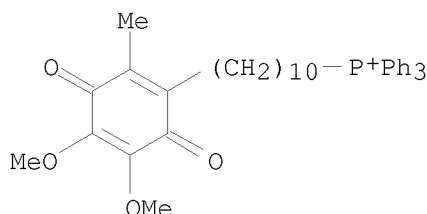
IT 444890-41-9P, MitoQ

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(as mitochondria-targeted antioxidant; reducing anthracycline-induced toxicity by coadministering mitochondria-targeted antioxidant)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



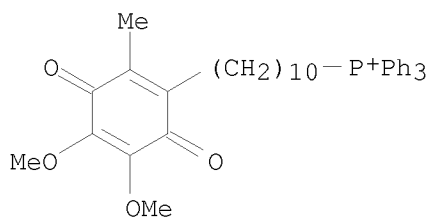
IT 336184-91-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as mitochondria-targeted antioxidant; reducing anthracycline-induced toxicity by coadministering mitochondria-targeted antioxidant)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



L3 ANSWER 43 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:90893 CAPLUS

DOCUMENT NUMBER: 148:192198

TITLE: Preparation of peptidomimetics as modulators of pharmacokinetic properties of therapeutics by inhibiting cytochrome P450 monooxygenase

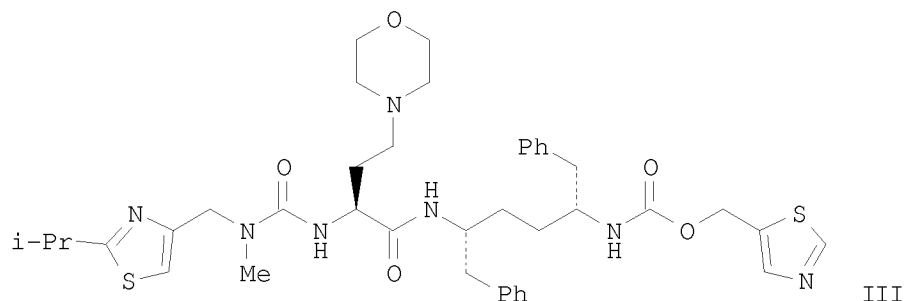
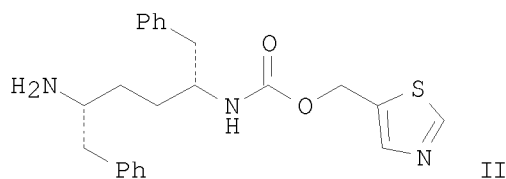
INVENTOR(S): Desai, Manoj C.; Hong, Allen Yu; Liu, Hongtao; Xu, Lianhong; Vivian, Randall W.



PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA  
 SOURCE: PCT Int. Appl., 346 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008010921	A2	20080124	WO 2007-US15604	20070706
WO 2008010921	A3	20080710		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2007275860	A1	20080124	AU 2007-275860	20070706
CA 2653374	A1	20080124	CA 2007-2653374	20070706
US 20080108617	A1	20080508	US 2007-825605	20070706
AR 61838	A1	20080924	AR 2007-103029	20070706
EP 2049506	A2	20090422	EP 2007-836007	20070706
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS			
JP 2009542696	T	20091203	JP 2009-518393	20070706
IN 2008DN10487	A	20100820	IN 2008-DN10487	20081218
CN 101490023	A	20090722	CN 2007-80025607	20090106
MX 2009000234	A	20090123	MX 2009-234	20090107
KR 2009028821	A	20090319	KR 2009-702544	20090206
NO 2009000593	A	20090407	NO 2009-593	20090206
HR 2009000077	A2	20090630	HR 2009-77	20090206
US 20090291952	A1	20091126	US 2009-306198	20090206
PRIORITY APPLN. INFO.:			US 2006-819315P	P 20060707
			US 2006-832371P	P 20060721
			US 2007-903228P	P 20070223
			WO 2007-US15604	W 20070706

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT  
 OTHER SOURCE(S): CASREACT 148:192198; MARPAT 148:192198  
 GI



AB The invention is related to the preparation of R8YZ1[CONR1(CR2R2)m]nL1NR3CH[L3A(L4Ar)p]CHR4L2CH[L3A(L4Ar)p]NR5COZ2XR9 [I; L1 = C(R6)2, CO, SO2, NHCO and derivs., OCO; R4, R6 = independently H, heteroalkyl, (un)substituted alkyl; L2 = a covalent bond, C(R6)2, CO; each L3 = independently a covalent bond, (un)substituted alkylene; each L4 = L3, O, CH2O, NH; each A = H, (un)substituted alkyl, aryl, heterocyclyl with the proviso that when A = H, p = 0; Z1, Z2 = independently O, NH and derivs.; Y, X = independently heterocyclyl, heterocyclylalkyl; each Ar = independently (un)substituted (hetero)aryl; R1, R3, R5 = independently H, (un)substituted aryl/alkyl; each R2 = independently H, (un)substituted arylhetero/hydroxy/amino/alkyl, alkylene-CO2H, alkylene-CO-alkyl, etc.; R8, R9 are each one or more H's or substituents selected from Cl, CN, (un)substituted alkyl, aryl, heterocyclyl; m = 1-2; n = 0-1; each p = independently 0-1], their pharmaceutically acceptable salts, solvates and esters, and compns. containing them which improve the pharmacokinetics of a co-administered drug which is metabolized by cytochrome P 450 monooxygenase. Thus, a multi-step synthesis using 2-isopropyl-4-[(methylamino)methyl]-1,3-thiazole, (2S)-2-amino-4-[(tert-butoxycarbonyl)amino]butanoic acid Me ester, amine II and (BrCH2CH2)2O was given for III. III inhibited CYP450 3A4 (IC50 = 80-150 nM), CYP450 2C9 (IC50 = 1,000-10,000 nM) and protease (EC50 > 20,000 nM in an anti HIV-1 cell culture assay). I alone or in combination with one or more addnl. therapeutic agents which are metabolized by cytochrome P 450 monooxygenase are useful for treating a viral infection, e.g. HIV (no data).

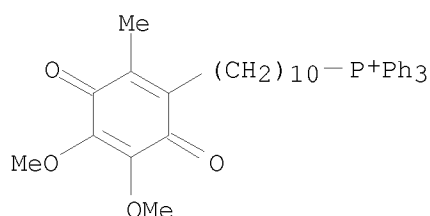
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compds. as modulators of pharmacokinetic properties of therapeutic agents)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD  
(3 CITINGS)

L3 ANSWER 44 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:62861 CAPLUS

DOCUMENT NUMBER: 148:182855

TITLE: Is Antioxidant Potential of the Mitochondrial Targeted Ubiquinone Derivative MitoQ Conserved in Cells Lacking mtDNA?

AUTHOR(S): Lu, Chao; Zhang, Dawei; Whiteman, Matthew; Armstrong, Jeffrey S.

CORPORATE SOURCE: Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

SOURCE: Antioxidants & Redox Signaling (2008), 10(3), 651-660  
CODEN: ARSIF2; ISSN: 1523-0864

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB MitoQ was developed as a mitochondrial targeted antioxidant for diseases associated with oxidative stress. Here we show that MitoQ blocks the generation of reactive oxygen species (ROS) and mitochondrial protein thiol oxidation, and preserves mitochondrial function and ultrastructure after glutathione (GSH) depletion. Furthermore, the antioxidant effect of MitoQ is conserved in cells lacking mitochondrial DNA, indicating that its antioxidant properties do not depend on a functional electron transport chain (ETC). Our results elucidate the antioxidant mechanism of MitoQ and suggest that it may be a useful therapeutic for disorders associated with a dysfunctional ETC and increased ROS production

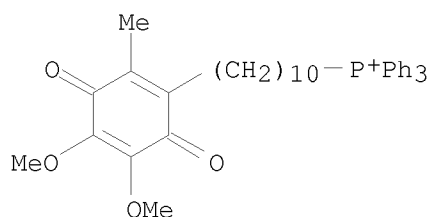
IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(MitoQ antioxidant effect via blocking ROS and protein thiol oxidation, and preserving mitochondria independently of glutathione and electron transport chain)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 45 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:40914 CAPLUS

DOCUMENT NUMBER: 148:168504

TITLE: Preparation of purine and thiadeazapurine phosphonate derivatives as modulators of toll-like receptor 7

INVENTOR(S): Chong, Lee S.; Desai, Manoj C.; Gallagher, Brian; Graupe, Michael; Halcomb, Randall L.; Yang, Hong; Zhang, Jennifer R.

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 273pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008005555	A1	20080110	WO 2007-US15615	20070706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007269557	A1	20080110	AU 2007-269557	20070706
CA 2656427	A1	20080110	CA 2007-2656427	20070706
US 20080008682	A1	20080110	US 2007-825377	20070706
AR 61839	A1	20080924	AR 2007-103030	20070706
EP 2038290	A1	20090325	EP 2007-836017	20070706
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
JP 2009542697	T	20091203	JP 2009-518395	20070706
US 20090202484	A1	20090813	US 2009-303214	20090219

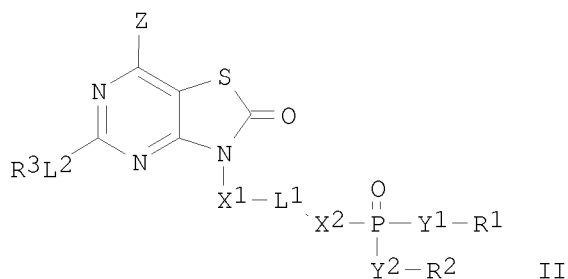
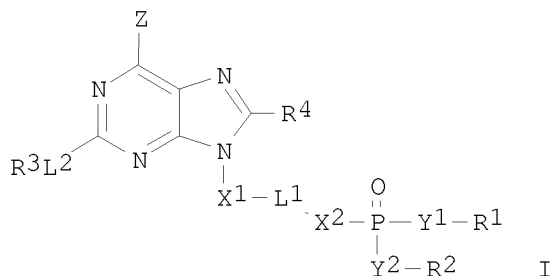
## PRIORITY APPLN. INFO.:

US 2006-819490P	P	20060707
US 2006-832851P	P	20060724
WO 2007-US15615	W	20070706

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

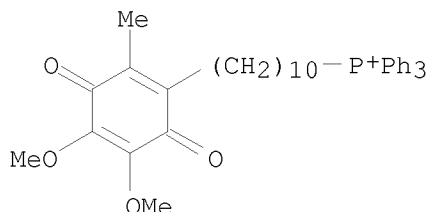
OTHER SOURCE(S): CASREACT 148:168504; MARPAT 148:168504

GI



AB The present application provides for a compound I [Z = OH, NH<sub>2</sub>; X<sub>1</sub> = (un)substituted alkylene, alkenylene, alkynylene, carbocyclylene, heterocyclylene; L<sub>1</sub> = bond, (un)substituted arylene, heterocyclylene, carbocyclylene, S, S(:O), SO<sub>2</sub>, NR<sub>5</sub>, O; X<sub>2</sub> = bond, (un)substituted alkylene; L<sub>2</sub> = NR<sub>5</sub>, NR<sub>5</sub>C(:O), O, S, S(:O), SO<sub>2</sub>, bond; R<sub>3</sub> = H, (un)substituted alkyl, heteroalkyl, alkenyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; Y<sub>1</sub>, Y<sub>2</sub> = bond, O, NR<sub>5</sub>, Y<sub>1</sub>R<sub>1</sub>, Y<sub>2</sub>R<sub>2</sub> = ON:CR<sub>6</sub>R<sub>7</sub>; R<sub>1</sub>, R<sub>2</sub> = H, (un)substituted alkyl, carbocyclyl, heterocyclyl, alkenyl, alkynyl, arylalkyl, etc.; R<sub>4</sub> = H, halogen, OH, O-alkyl, O-alkylene-OCOR<sub>5</sub>, OCOR<sub>5</sub>, SH, NHR<sub>5</sub>; R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> = H, (un)substituted alkyl, carbocyclyl, heterocyclyl, alkenyl, alkynyl, arylalkyl, heterocyclylalkyl, etc.] or II or a pharmaceutically acceptable salt, solvate, and/or ester thereof, compns. containing such compds., therapeutic methods that include the administration of such compds., and therapeutic methods that include the administration of such compds. with at least one addnl. active agent. Thus, [(3-((6-amino-8-hydroxy-2-(2-methoxyethoxy)-9H-purin-9-yl)methyl)phenyl)methyl](methyl)phosphinic acid [I; Z = NH<sub>2</sub>, R<sub>4</sub> = OH, L<sub>2</sub> = O, R<sub>3</sub> = CH<sub>2</sub>CH<sub>2</sub>OMe, X<sub>1</sub> = X<sub>2</sub> = CH<sub>2</sub>, L<sub>1</sub> = 1,3-phenylene, Y<sub>1</sub>R<sub>1</sub> = Me, Y<sub>2</sub>R<sub>2</sub> = OH] was prepared from 6-chloroadenine via N-alkylation with 3-(BrCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me, alkoxylation with MeOCH<sub>2</sub>CH<sub>2</sub>OH, reesterification with MeI, bromination with Br<sub>2</sub>, Dibal-H reduction, methanolysis with NaOMe/MeOH, acid hydrolysis, bromination with PBr<sub>3</sub>, phosphorylation with MeP(OEt)<sub>2</sub> and acid hydrolysis under microwave irradiation The toll-like receptor 7

modulating activity of I and II were investigated (no data).  
IT 444890-41-9, MitoQ  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(compds. as modulators of Toll-like receptor 7 useful in combination  
therapy and prevention of TLR7 activation-related diseases)  
RN 444890-41-9 CAPLUS  
CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD  
(3 CITINGS)

L3 ANSWER 46 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:1220757 CAPLUS

DOCUMENT NUMBER: 148:2715

TITLE: Mitochondrial redox cycling of mitoquinone leads to  
superoxide production and cellular apoptosis

AUTHOR(S): Doughan, Abdulrahman K.; Dikalov, Sergey I.

CORPORATE SOURCE: Free Radical in Medicine Core, Division of Cardiology,  
Emory University School of Medicine, Atlanta, GA, USA

SOURCE: Antioxidants & Redox Signaling (2007), 9(11),  
1825-1836

CODEN: ARSIF2; ISSN: 1523-0864

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mitochondria-targeted drug mitoquinone (MitoQ) has been used as an antioxidant that may selectively block mitochondrial oxidative damage; however, it has been recently suggested to increase reactive oxygen species (ROS) generation in malate- and glutamate-fueled mitochondria. To address this controversy, we studied the effects of MitoQ on endothelial and mitochondrial ROS production. We found that in a cell-free system with flavin-containing enzyme cytochrome P 450 reductase, MitoQ is a very efficient redox cycling agent and produced more superoxide compared with equal concns. of menadione (10-1000 nM). Treatment of endothelial cells with MitoQ resulted in a dramatic increase in superoxide production. In isolated mitochondria, MitoQ increased complex I-driven mitochondrial ROS production, whereas supplementation with ubiquinone-10 had no effect on ROS production. Similar results were observed in mitochondria isolated from endothelial cells incubated for 1 h with MitoQ. Inhibitor anal. suggested that the redox cycling of MitoQ occurred at two sites on complex I, proximal and distal to the rotenone-binding site. This was confirmed by demonstrating the redox cycling of MitoQ on purified mitochondrial complex I as well as NADH-fueled submitochondrial particles. Mitoquinone time- and dose-dependently increased endothelial cell apoptosis. These findings

demonstrate that MitoQ may be prooxidant and proapoptotic because its quinone group can participate in redox cycling and superoxide production. In light of these results, studies using mitoquinone as an antioxidant should be interpreted with caution.

IT 845959-50-4

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(mitochondrial redox cycling of mitoquinone leads to superoxide production and cellular apoptosis)

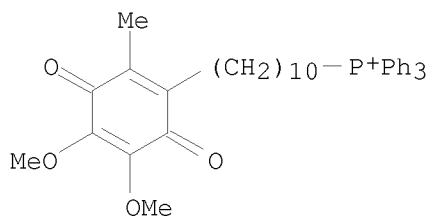
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

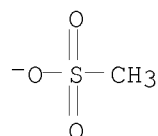
CMF C37 H44 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)  
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 47 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:1030540 CAPLUS

DOCUMENT NUMBER: 147:481558

TITLE: Mitochondrial uncouplers with an extraordinary dynamic range

AUTHOR(S): Lou, Phing-How; Hansen, Birgit S.; Olsen, Preben H.; Tullin, Soren; Murphy, Michael P.; Brand, Martin D.

CORPORATE SOURCE: MRC Dunn Human Nutrition Unit, Cambridge, CB2 2XY, UK  
SOURCE: Biochemical Journal (2007), 407(1), 129-140

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have discovered that some weak uncouplers (typified by butylated hydroxytoluene) have a dynamic range of more than 10<sup>6</sup> in vitro: the concentration

giving measurable uncoupling is less than one millionth of the concentration causing full uncoupling. They achieve this through a high-affinity interaction with the mitochondrial adenine nucleotide translocase that causes significant but limited uncoupling at extremely low uncoupler concns., together with more conventional uncoupling at much higher concns. Uncoupling at the translocase is not by a conventional weak acid/anion cycling mechanism since it is also caused by substituted triphenylphosphonium mols., which are not anionic and cannot protonate. Covalent attachment of the uncoupler to a mitochondrially targeted hydrophobic cation sensitizes it to membrane potential, giving a small addnl. effect. The wide dynamic range of these uncouplers in isolated mitochondria and intact cells reveals a novel allosteric activation of proton transport through the adenine nucleotide translocase and provides a promising starting point for designing safer uncouplers for obesity therapy.

IT 845959-50-4 845959-58-2 954111-83-2

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(mitochondrial uncouplers with extraordinary dynamic range)

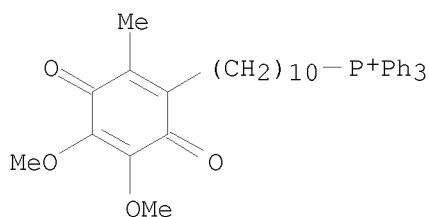
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

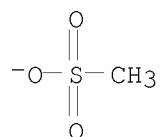
CMF C37 H44 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S





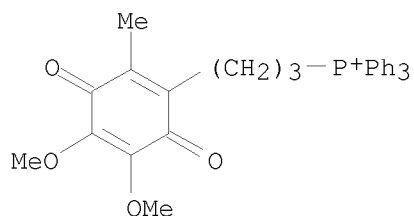
RN 845959-58-2 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 794485-93-1

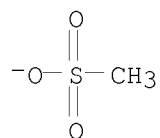
CMF C30 H30 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



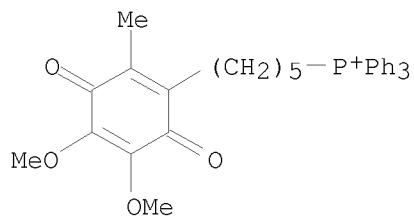
RN 954111-83-2 CAPLUS

CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 794485-94-2

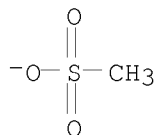
CMF C32 H34 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS  
RECORD (11 CITINGS)  
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 48 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:965666 CAPLUS

DOCUMENT NUMBER: 148:135860

TITLE: Mitochondria-targeted antioxidants do not prevent  
tumor necrosis factor-induced necrosis of L929 cellsAUTHOR(S): Jarvis, Reagan M.; Goetttert, Jana; Murphy, Michael P.;  
Ledgerwood, Elizabeth C.CORPORATE SOURCE: Department of Biochemistry, University of Otago,  
Dunedin, N. Z.SOURCE: Free Radical Research (2007), 41(9), 1041-1046  
CODEN: FRARER; ISSN: 1071-5762

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal

LANGUAGE: English

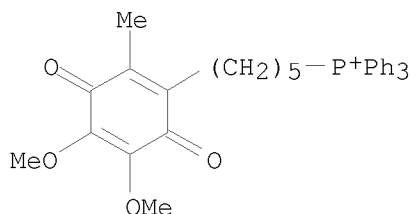
AB Mitochondrial production of reactive oxygen species (ROS) is widely reported as a central effector during TNF-induced necrosis. The effect of a family of mitochondria-targeted antioxidants on TNF-induced necrosis of L929 cells was studied. While the commonly used lipid-soluble antioxidant BHA effectively protected cells from TNF-induced necrosis, the mitochondria-targeted antioxidants MitoQ3, MitoQ5, MitoQ10 and MitoPBN had no effect on TNF-induced necrosis. Since BHA also acts as an uncoupler of mitochondrial membrane potential, two addnl. uncouplers were tested. FCCP and CCCP both provided dose-dependent inhibition of TNF-induced necrosis. In conclusion, the generation of mitochondrial ROS may not be necessary for TNF-induced necrosis. Instead, these results suggest alternative mitochondrial functions, such as a respiration-dependent process, are critical for necrotic death.

IT 764723-90-2 845959-57-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)(mitochondria-targeted antioxidants do not prevent tumor necrosis  
factor-induced necrosis of L929 cells)

RN 764723-90-2 CAPLUS

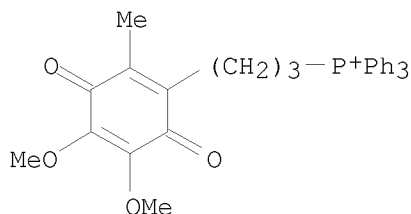
CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl-, iodide (1:1) (CA INDEX NAME)



● I<sup>-</sup>

RN 845959-57-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



● Br<sup>-</sup>

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 49 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:922908 CAPLUS

DOCUMENT NUMBER: 147:356077

TITLE: Targeting antioxidants to mitochondria and cardiovascular diseases: the effects of mitoquinone

AUTHOR(S): Rocha, Milagros; Victor, Victor Manuel

CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Universitat of Valencia, Valencia, Spain

SOURCE: Medical Science Monitor (2007), 13(7), RA132-RA145  
CODEN: MSMOFR; ISSN: 1234-1010

PUBLISHER: International Scientific Literature, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Mitochondria have long been known to play a critical role in maintaining the bioenergetic status of cells under physiol. conditions. Mitochondria produce large amts. of free radicals, and mitochondrial oxidative damage can contribute to a range of degenerative conditions including cardiovascular diseases (CVDs). Although the mol. mechanisms

responsible for mitochondrion-mediated disease processes are not correctly understood, oxidative stress seems to play an important role. Consequently, the selective inhibition of mitochondrial oxidative damage is an obvious therapeutic strategy. This review considers the process of CVD from a mitochondrial perspective and provides a summary of the following areas: reactive oxygen species (ROS) production and its role in pathophysiol. processes such as CVD, currently available antioxidants and possible reasons for their efficacy and inefficacy in ameliorating oxidative stress-mediated diseases, and recent developments in mitochondria-targeted antioxidants that concentrate on the matrix-facing

surface

of the inner mitochondrial membrane. These mitochondrion-targeted antioxidants have been developed by conjugating the lipophilic triphenylphosphonium cation to antioxidant moieties such as ubiquinol. These compds. pass easily through biol. membranes and, due to their pos. charge, they accumulate several-hundred-fold within mitochondria. In this way they protect against mitochondrial oxidative damage and show potential as a future therapy for CVDs.

IT 845959-50-4, Mitoquinone

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(loss of control of reactive oxygen species formation in mitochondria leads to pathol. of cardiovascular disease in animals and mitoquinone protect against mitochondrial oxidative damage and showed potential as future therapy for CVD)

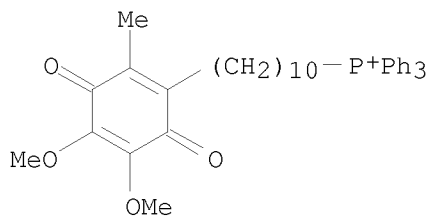
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

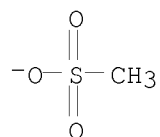
CMF C37 H44 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)  
REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 50 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:818711 CAPLUS

DOCUMENT NUMBER: 147:335184

TITLE: Drug evaluation: MitoQ - a mitochondrial-targeted antioxidant

AUTHOR(S): Tauskela, Joseph S.

CORPORATE SOURCE: Institute for Biological Sciences, Synaptic Pathophysiology Group, National Research Council, Ottawa, ON, K1A 0R6, Can.

SOURCE: IDrugs (2007), 10(6), 399-412  
CODEN: IDRUFN; ISSN: 1369-7056

PUBLISHER: Thomson Scientific

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

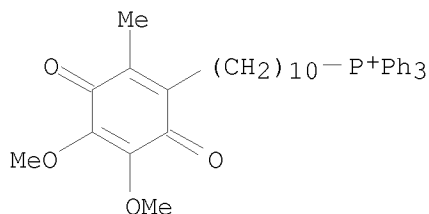
AB A review. MitoQ is an orally active antioxidant that has the ability to target mitochondrial dysfunction. The agent is currently under development by Antipodean Pharmaceuticals Inc and is in phase II clin. trials for Parkinson's disease and liver damage associated with HCV infection. MitoQ demonstrated encouraging preclin. results in numerous studies in isolated mitochondria, cells and tissues undergoing oxidative stress and apoptotic death. The aim of MitoQ is to not only mimic the role of the endogenous mitochondrial antioxidant coenzyme Q10 (CoQ10), but also to substantially augment the antioxidant capacity of the coenzyme to supraphysiol. levels in a mitochondrial membrane potential-dependent manner. MitoQ represents the first foray into the clinic of an attempt to deliver an antioxidant to an intracellular region that is responsible for the formation of increased levels of potentially deleterious reactive oxygen species. Results from the clin. trials with MitoQ will have important repercussions regarding the relevance of a mitochondria-targeted approach.

IT 444890-41-9, MitoQ

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mitochondrial-targeted antioxidant MitoQ)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)  
REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 51 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:739270 CAPLUS

DOCUMENT NUMBER: 147:273456

TITLE: Quantitation and metabolism of mitoquinone, a mitochondria-targeted antioxidant, in rat by liquid chromatography/tandem mass spectrometry

AUTHOR(S): Li, Yan; Zhang, Hu; Fawcett, J. Paul; Tucker, Ian G.  
CORPORATE SOURCE: School of Pharmacy, University of Otago, Dunedin, N. Z.

SOURCE: Rapid Communications in Mass Spectrometry (2007), 21(13), 1958-1964

CODEN: RCMSEF; ISSN: 0951-4198

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mitoquinone (MitoQ10 mesylate) is a mitochondria-targeted antioxidant undergoing development for the treatment of neurodegenerative diseases. The aim of this study was to develop and validate an assay based on liquid chromatog./tandem mass spectrometry (LC/MS/MS) to determine mitoquinone and to detect and identify the metabolites of MitoQ10 in rat plasma after an oral dose. After a simple protein precipitation step, plasma samples were analyzed by

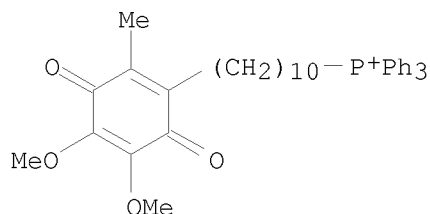
reversed-phase liquid chromatog. using gradient elution with acetonitrile/water/formic acid. Electrospray ionization in the pos. ion mode with multiple reaction monitoring (MRM) was used to analyze mitoquinone employing the deuterated compound (d3-MitoQ10 mesylate) as internal standard. The calibration curve for mitoquinone was linear over the concentration range 0.5-250 ng/mL with a correlation coefficient >0.995. The method

was sensitive (limit of quantitation 0.5 ng/mL) and had acceptable accuracy (relative error <8.7%) and precision (intra- and inter-day coefficient of variation <12.4%). Recoveries of mitoquinone at concns. of 1.5, 20 and 200 ng/mL were in the range 87-114%. The method was successfully applied to a pharmacokinetic study in rat after a single oral dose in which four metabolites of MitoQ10 were tentatively identified as hydroxylated MitoQ10, desmethyl MitoQ10 and the glucuronide and sulfate conjugates of the quinol form of MitoQ10.

IT 444890-41-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(quantitation and metabolism of mitochondria-targeted antioxidant mitoquinone in rat)

RN 444890-41-9 CAPLUS  
CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)  
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 52 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:542355 CAPLUS

DOCUMENT NUMBER: 147:157119

TITLE: Targeting antioxidants to mitochondria: a potential new therapeutic strategy for cardiovascular diseases

AUTHOR(S): Victor, V. M.; Rocha, M.

CORPORATE SOURCE: Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, 28029, Spain

SOURCE: Current Pharmaceutical Design (2007), 13(8), 845-863  
CODEN: CPDEFP; ISSN: 1381-6128

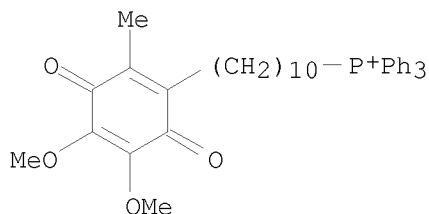
PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Mitochondria produce large amts. of free radicals and play an important role in the life and death of a cell. Thus, mitochondrial oxidative damage and dysfunction contribute to a number of cell pathologies that manifest themselves through a range of conditions including ischemia-reperfusion injury, sepsis, diabetes, atherosclerosis and, consequently, cardiovascular diseases (CVD). In fact, endothelial dysfunction, characterized by a loss of nitric oxide (NO) bioactivity, occurs early on in the development of atherosclerosis, and dets. future vascular complications. Although the mol. mechanisms responsible for mitochondria-mediated disease processes are not yet clear, oxidative stress seems to play an important role. This review considers the process of CVD from a mitochondrial perspective. Accordingly, strategies for the targeted delivery of antioxidants to mitochondria are being developed. In this review, we will provide a summary of the following areas: the cellular metabolism of reactive oxygen species (ROS) and its role in pathophysiol. processes such as CVD; currently available antioxidants and possible reasons for their efficacy and inefficacy in ameliorating oxidative stress-mediated diseases; recent developments in mitochondrially-targeted antioxidants that concentrate on the matrix-facing surface of the inner mitochondrial membrane and therefore protect against mitochondrial oxidative damage, and their therapeutic potential for future treatment of CVDs. More pre-clin. and clin. studies, however, are necessary in order to evaluate the effectiveness and toxicity of mitochondrially-targeted antioxidants.

IT 444890-41-9, MitoQ  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (targeting antioxidants to mitochondria with a potential new therapeutic strategy for cardiovascular diseases)  
 RN 444890-41-9 CAPLUS  
 CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)  
 REFERENCE COUNT: 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L3 ANSWER 53 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:522753 CAPLUS

DOCUMENT NUMBER: 147:202729

TITLE: Mitochondrial targeting of quinones: Therapeutic implications

AUTHOR(S): Cocheme, Helena M.; Kelso, Geoffrey F.; James, Andrew M.; Ross, Meredith F.; Trnka, Jan; Mahendiran, Thabo; Asin-Cayuela, Jordi; Blaikie, Frances H.; Manas, Abdul-Rahman B.; Porteous, Carolyn M.; Adlam, Victoria J.; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: MRC Dunn Human Nutrition Unit, Cambridge, CB2 2XY, UK  
 SOURCE: Mitochondrion (2007), 7(Suppl.), S94-S102  
 CODEN: MITOCN; ISSN: 1567-7249

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Mitochondrial oxidative damage contributes to a range of degenerative diseases. Ubiquinones have been shown to protect mitochondria from oxidative damage, but only a small proportion of externally administered ubiquinone is taken up by mitochondria. Conjugation of the lipophilic triphenylphosphonium cation to a ubiquinone moiety has produced a compound, MitoQ, which accumulates selectively into mitochondria. MitoQ passes easily through all biol. membranes and, because of its pos. charge, is accumulated several hundred-fold within mitochondria driven by the mitochondrial membrane potential. MitoQ protects mitochondria against oxidative damage in vitro and following oral delivery, and may therefore form the basis for mitochondria-protective therapies.

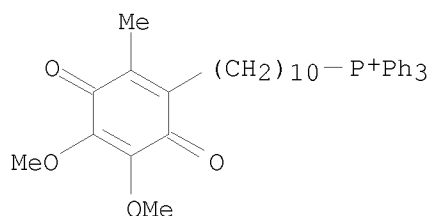
IT 444890-41-9, MitoQ  
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)



(mitochondrial targeting of quinones and therapeutic implications)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)  
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 54 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:513564 CAPLUS

DOCUMENT NUMBER: 147:160001

TITLE: Interaction of the Mitochondria-targeted Antioxidant MitoQ with Phospholipid Bilayers and Ubiquinone Oxidoreductases

AUTHOR(S): James, Andrew M.; Sharples, Mark S.; Manas, Abdul-Rahman B.; Frerman, Frank E.; Hirst, Judy; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: Medical Research Council Dunn Human Nutrition Unit, Cambridge, CB2 2XY, UK

SOURCE: Journal of Biological Chemistry (2007), 282(20), 14708-14718

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB MitoQ10 is a ubiquinone that accumulates within mitochondria driven by a conjugated lipophilic triphenylphosphonium cation (TPP+). Once there, MitoQ10 is reduced to its active ubiquinol form, which has been used to prevent mitochondrial oxidative damage and to infer the involvement of reactive oxygen species in signaling pathways. Here we show MitoQ10 is effectively reduced by complex II, but is a poor substrate for complex I, complex III, and electron-transferring flavoprotein (ETF):quinone oxidoreductase (ETF-QOR). This differential reactivity could be explained if the bulky TPP+ moiety sterically hindered access of the ubiquinone group to enzyme active sites with a long, narrow access channel. Using a combination of mol. modeling and an uncharged analog of MitoQ10 with similar sterics (tritylQ10), we infer that the interaction of MitoQ10 with complex I and ETF-QOR, but not complex III, is inhibited by its bulky TPP+ moiety. To explain its lack of reactivity with complex III we show that the TPP+ moiety of MitoQ10 is ineffective at quenching pyrene fluorophors deeply buried within phospholipid bilayers and thus is positioned near the membrane surface. This superficial position of the TPP+ moiety, as well as the low solubility of MitoQ10 in non-polar organic solvents, suggests that the

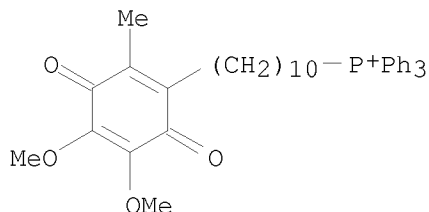
concentration of the entire MitoQ10 mol. in the membrane core is very limited. As overlaying MitoQ10 onto the structure of complex III indicates that MitoQ10 cannot react with complex III without its TPP+ moiety entering the low dielec. of the membrane core, we conclude that the TPP+ moiety does anchor the tethered ubiquinol group out of reach of the active site(s) of complex III, thus explaining its slow oxidation. In contrast the ubiquinone moiety of MitoQ10 is able to quench fluorophors deep within the membrane core, indicating a high concentration of the ubiquinone moiety within the membrane and explaining its good anti-oxidant efficacy. These findings will facilitate the rational design of future mitochondria-targeted mols.

IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(interaction of mitochondria-targeted antioxidant MitoQ with  
phospholipid bilayers and ubiquinone oxidoreductases)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS  
RECORD (33 CITINGS)  
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 55 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:407185 CAPLUS

DOCUMENT NUMBER: 147:63256

TITLE: Transport and metabolism of MitoQ10, a  
mitochondria-targeted antioxidant, in Caco-2 cell  
monolayers

AUTHOR(S): Li, Yan; Fawcett, J. Paul; Zhang, Hu; Tucker, Ian G.

CORPORATE SOURCE: School of Pharmacy, University of Otago, Dunedin, N.  
Z.

SOURCE: Journal of Pharmacy and Pharmacology (2007), 59(4),  
503-511

CODEN: JPPMAB; ISSN: 0022-3573

PUBLISHER: Pharmaceutical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 147:63256

AB Mitoquinone (MitoQ10 mesylate) is a mitochondria-targeted antioxidant formulated for oral administration in the treatment of neurodegenerative diseases. We have investigated the absorption and metabolism of MitoQ10 in Caco-2 cell monolayers. The intracellular accumulation of MitoQ10 was 18-41% of the total amount of MitoQ10 added. Some of the intracellular MitoQ10 was reduced to mitoquinol and subsequently metabolized to glucuronide and sulfate conjugates. Transport of MitoQ10 was polarized

with the apparent permeability (Papp) from basolateral (BL) to apical (AP) (PappBL→AP) being >2.5-fold the Papp from apical to basolateral (PappAP→BL). In the presence of 4% bovine serum albumin on the basolateral side, the PappAP→BL value increased 7-fold compared with control. The PappBL→AP value decreased by 26%, 31%, and 61% in the presence of verapamil 100  $\mu$ M, ciclosporin 10 and 30  $\mu$ M, resp., whereas the PappAP→BL value increased 71% in the presence of ciclosporin 30  $\mu$ M. Apical efflux of mitoquinol sulfate and mitoquinol glucuronide conjugates was significantly decreased by ciclosporin 30  $\mu$ M and the breast cancer receptor protein (BCRP) inhibitor, reserpine 25  $\mu$ M, resp. These results suggested that the bioavailability of MitoQ10 may be limited by intracellular metabolism and the action of P-glycoprotein and BCRP. However, the dramatic increase in absorptive Papp in the presence of bovine serum albumin on the receiver side suggests these barrier functions may be less significant in-vivo.

IT 845959-50-4, Mitoquinone mesylate

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(transport and metabolism of MitoQ10 as mitochondria-targeted antioxidant, in Caco-2 cell monolayers)

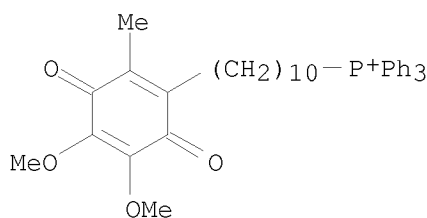
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

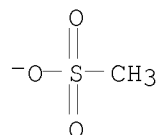
CMF C37 H44 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 56 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:70572 CAPLUS

DOCUMENT NUMBER: 146:182912

TITLE: High Concentration of Antioxidants N-Acetylcysteine and Mitoquinone-Q Induces Intercellular Adhesion Molecule 1 and Oxidative Stress by Increasing Intracellular Glutathione

AUTHOR(S): Mukherjee, Tapan K.; Mishra, Anurag K.; Mukhopadhyay, Srirupa; Hoidal, John R.

CORPORATE SOURCE: Department of Internal Medicine, Pulmonary Division, University of Utah Health Science Center, Salt Lake City, UT, 84112, USA

SOURCE: Journal of Immunology (2007), 178(3), 1835-1844

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In endothelial cells, the intracellular level of glutathione is depleted during offering protection against proinflammatory cytokine TNF- $\alpha$ -induced oxidative stress. Administration of anti-inflammatory drugs, i.e., N-acetylcysteine (NAC) or mitoquinone-Q (mito-Q) in low concns. in the human pulmonary aortic endothelial cells offered protection against depletion of reduced glutathione and oxidative stress mediated by TNF- $\alpha$ . However, this study addressed that administration of NAC or mito-Q in high concns. resulted in a biphasic response by initiating an enhanced generation of both reduced glutathione and oxidized glutathione and enhanced production of reactive oxygen species, along with carbonylation and glutathionylation of the cellular proteins. This study further addressed that I $\kappa$ B kinase (IKK), a phosphorylation-dependent regulator of NF- $\kappa$ B, plays an important regulatory role in the TNF- $\alpha$ -mediated induction of the inflammatory cell surface mol. ICAM-1. Of the two catalytic subunits of IKK (IKK $\alpha$  and IKK $\beta$ ), low concns. of NAC and mito-Q activated IKK $\alpha$  activity, thereby inhibiting the downstream NF- $\kappa$ B and ICAM-1 induction by TNF- $\alpha$ . High concns. of NAC and mito-Q instead caused glutathionylation of IKK $\alpha$ , thereby inhibiting its activity that in turn enhanced the downstream NF- $\kappa$ B activation and ICAM-1 expression by TNF- $\alpha$ . Thus, establishing IKK $\alpha$  as an anti-inflammatory mol. in endothelial cells is another focus of this study. This is the first report that describes a stressful situation in the endothelial cells created by excess of antioxidative and anti-inflammatory agents NAC and mito-Q, resulting in the generation of reactive oxygen species, carbonylation and glutathionylation of cellular proteins, inhibition of IKK $\alpha$  activity, and up-regulation of ICAM-1 expression.

IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); BIOL (Biological study)

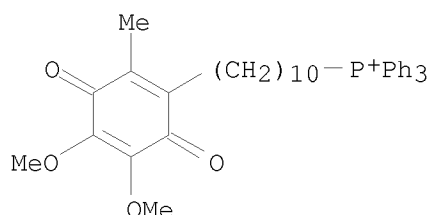
(high concentration of antioxidants N-acetylcysteine and mitoquinone-Q

induces

ICAM-1 and oxidative stress by increasing intracellular glutathione)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)  
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 57 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:1348478 CAPLUS

DOCUMENT NUMBER: 146:178916

TITLE: Reactive Oxygen and Targeted Antioxidant

Administration in Endothelial Cell Mitochondria

AUTHOR(S): O'Malley, Yunxia; Fink, Brian D.; Ross, Nicolette C.;  
Prisinzano, Thomas E.; Sivitz, William I.

CORPORATE SOURCE: Iowa City Veterans Affairs Medical Center, Department  
of Internal Medicine, Division of Endocrinology and  
Metabolism and the College of Pharmacy, Division of  
Medicinal and Natural Products Chemistry, University  
of Iowa, Iowa City, IA, 52242, USA

SOURCE: Journal of Biological Chemistry (2006), 281(52),  
39766-39775

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular  
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We used fluorescent probes and EPR to study the mechanism(s) underlying reactive oxygen species (ROS) production by endothelial cell mitochondria and the action of mitoquinol (MitoQ), a mitochondria-targeted antioxidant. ROS measured by fluorescence resulted from complex I superoxide released to the matrix and converted to H<sub>2</sub>O<sub>2</sub>. In contrast, EPR largely detected superoxide generated at complex III and effluxed outward. ROS fluorescence by mitochondria fueled by the complex II substrate, succinate, was substantial but markedly inhibited by rotenone. Superoxide, detected by EPR, in succinate-fueled mitochondria was not inhibited by rotenone and likely derived from semiquinone formation at complex III. Mitoquinol decreased H<sub>2</sub>O<sub>2</sub> fluorescence by succinate-fueled mitochondria but had little effect on the EPR signal for superoxide. This was not associated with a detectable decrease in membrane potential. Mitoquinol markedly enhanced ROS fluorescence in mitochondria fueled by the complex I substrates, glutamate and malate. Inhibitor studies suggested that this occurred in complex I, at one or more Q binding pockets. The above effects of mitoquinol were determined in mitochondria isolated and subsequently exposed to the targeted antioxidant. However, similar effects were observed in mitochondria after antecedent exposure to mitoquinol/mitoquinone in culture, suggesting that the agent is retained after isolation of the organelles. In conclusion, ROS production in bovine aortic endothelial cell mitochondria results largely from reverse

transport to complex I and through the Q cycle in complex III. Mitoquinol blocks ROS from reverse electron transport but increases superoxide production derived from forward transport. These effects likely occur at one or more Q binding sites in complex I.

IT 444890-41-9, MitoQ

RL: BSU (Biological study, unclassified); BIOL (Biological study)

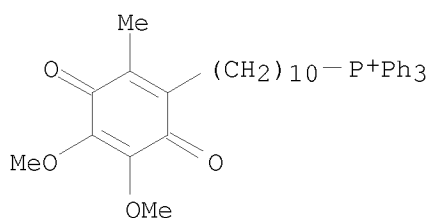
(MitoQ acts in complex I to block ROS generated by reverse electron

transport but increases superoxide production associated with forward electron

transport)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 58 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:1112822 CAPLUS

DOCUMENT NUMBER: 145:495544

TITLE: Antitumor sustained-release injection containing taxane and its synergistic agent

INVENTOR(S): Liu, Yuyan

PATENT ASSIGNEE(S): Jinan Kangquan Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CN 1846689	A	20061018	CN 2006-10200114	20060210
PRIORITY APPLN. INFO.:			CN 2006-10200114	20060210

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is taxane and/or the taxane synergistic agent which is selected from antimitotic drugs, alkylating agents and/or antimetabolite agents. The taxane is selected from taxol, docetaxel, paclitaxel-2'-hydroxy, 10-deacetylbaccatin III, and 7-epi-taxol. The antimitotic drug is selected from one of

podophyllotoxin, mitonafide, mitotane, colchicine, colchisal, naphthol, cytochalasin, etc., or the mixture thereof. The alkylating agent is selected from one of cyclophosphamide, melphalan, chlorambucil, ifosfamide, etc., or the mixture thereof. The antimetabolite agent is selected from one of 6-mercaptopurine, 5-fluorouracil, alimta, alimta disodium, etc., or the mixture thereof. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer; and (h) xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; or (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; or the mixture thereof. Said sustained-release preparation can

reduce

toxic reaction, at the same time can increase selectively drug concentration, and

enhance therapeutic effectiveness.

IT 444890-41-9, Mito-Q

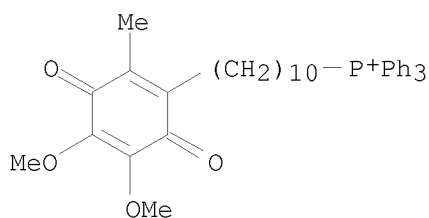
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(antitumor sustained-release injection containing taxane and its synergistic agent)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



L3 ANSWER 59 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:1067714 CAPLUS

DOCUMENT NUMBER: 145:419306

TITLE: Preparation of mitoquinone derivatives as mitochondrially targeted antioxidants

INVENTOR(S): Taylor, Kenneth Martin; Smith, Robin A. J.

PATENT ASSIGNEE(S): Antipodean Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 57pp., Cont.-in-part of U.S. Ser. No. 172,916.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

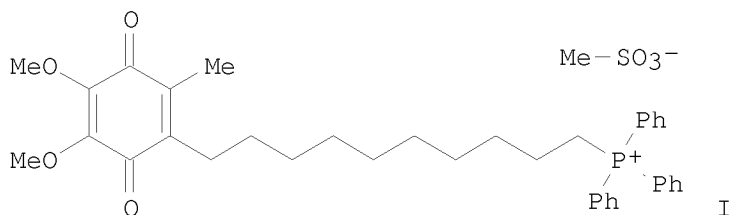
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US 20060229278	A1	20061012	US 2006-355518	20060215
WO 9926954	A1	19990603	WO 1998-NZ173	19981125
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US 6331532	B1	20011218	US 2000-577877	20000525
US 20020052342	A1	20020502	US 2001-968838	20011003
US 20030069208	A1	20030410	US 2002-272914	20021018
NZ 547101	A	20090731	NZ 2003-547101	20030822
US 20040106579	A1	20040603	US 2003-722542	20031128
WO 2005019232	A1	20050303	WO 2004-NZ196	20040823
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US 20050245487	A1	20051103	US 2005-172916	20050705
US 7232809	B2	20070619		
PRIORITY APPLN. INFO.:			WO 1998-NZ173	A2 19981125
			US 2000-577877	A1 20000525
			US 2001-968838	B1 20011003
			US 2002-272914	B1 20021018
			NZ 2003-527800	A 20030822
			NZ 2003-529153	A 20031023
			US 2003-722542	B1 20031128
			NZ 2004-533556	A 20040614
			WO 2004-NZ196	A1 20040823
			US 2005-172916	A2 20050705
			NZ 1997-329255	A 19971125

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S):

CASREACT 145:419306; MARPAT 145:419306

GI





AB This invention relates to pharmaceutically acceptable amphiphilic antioxidant compds., compns. and dosage forms comprising the compds. The compds., compns., dosage forms, uses and methods are useful in the treatment of diseases or conditions associated with oxidative stress. Thus, I 1:2 complex  $\beta$ -cyclodextrin with was prepared, and tested for stability and pharmacokinetics.

IT 845959-56-0P  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of mitoquinone triphenylphosphonium derivs. as mitochondrially targeted antioxidants)

RN 845959-56-0 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (2:1) (9CI)  
(CA INDEX NAME)

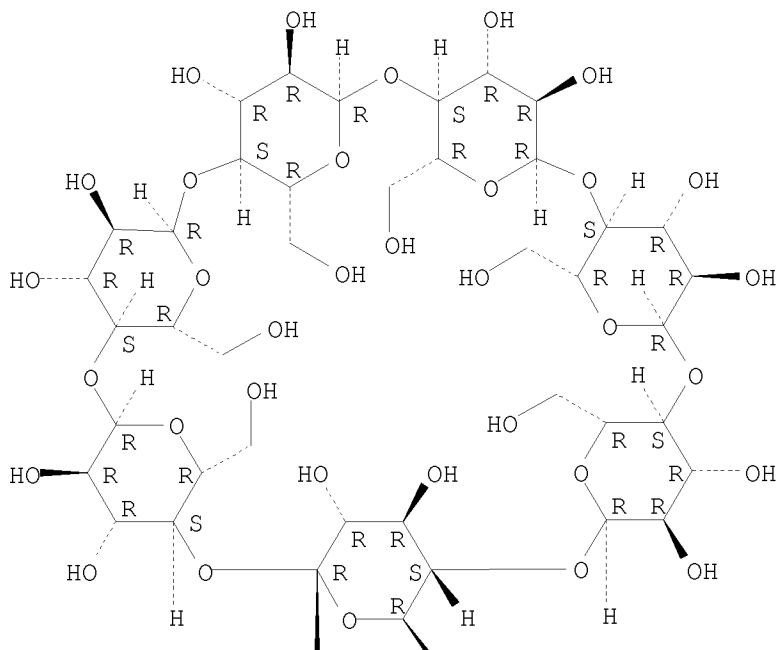
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CRN 7585-39-9

CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



CM 2

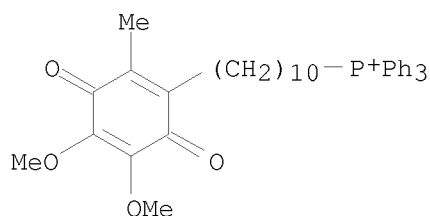
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CMF C37 H44 O4 P . C H3 O3 S

CM 3

CRN 444890-41-9

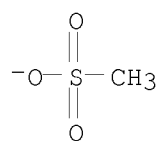
CMF C37 H44 O4 P



CM 4

CRN 16053-58-0

CMF C H3 O3 S



IT 845959-52-6P 911841-84-4P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of mitoquinone triphenylphosphonium derivs. as mitochondrially targeted antioxidants)

RN 845959-52-6 CAPLUS

CN β-Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (1:1) (9CI)  
(CA INDEX NAME)

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10568655

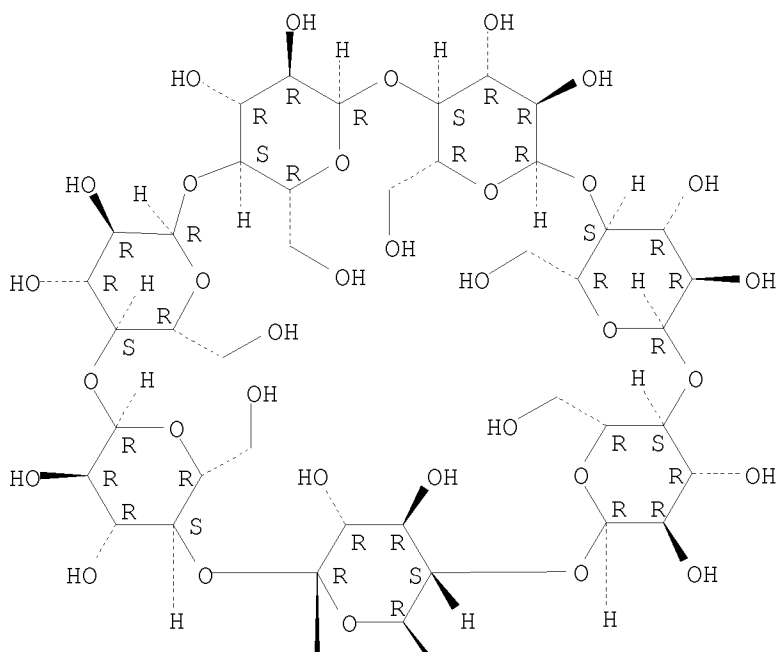
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STN: SEARCH

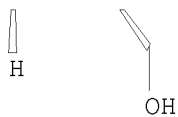
CRN 7585-39-9  
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

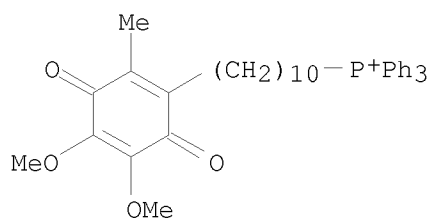


CM 2

CRN 845959-50-4  
CMF C37 H44 O4 P . C H3 O3 S

CM 3

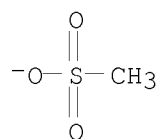
CRN 444890-41-9  
CMF C37 H44 O4 P



CM 4

CRN 16053-58-0

CMF C H3 O3 S



RN 911841-84-4 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (4:1) (9CI)  
(CA INDEX NAME)

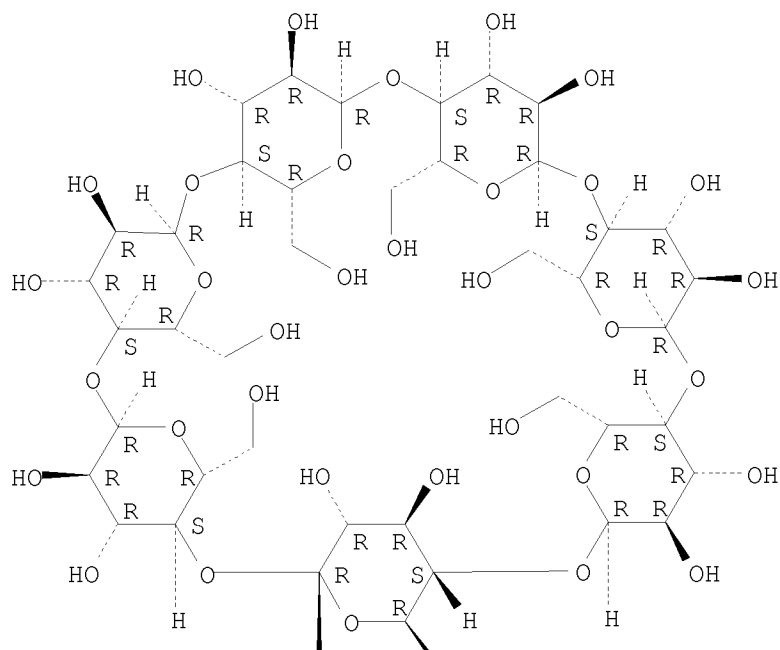
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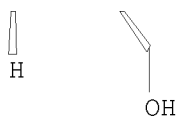
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



CM 2

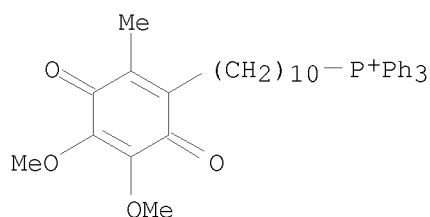
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CMF C37 H44 O4 P . C H3 O3 S

CM 3

CRN 444890-41-9

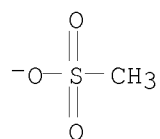
CMF C37 H44 O4 P



CM 4

CRN 16053-58-0

CMF C H3 O3 S



IT 845959-50-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of mitoquinone triphenylphosphonium derivs. as mitochondrially targeted antioxidants)

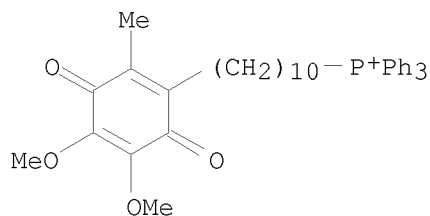
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

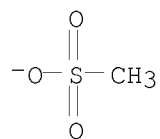
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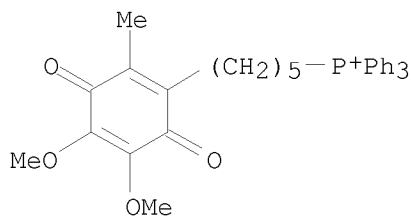
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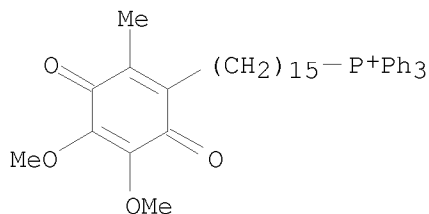
CMF C H3 O3 S



IT 764723-90-2P 764723-92-4P 845959-58-2P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of mitoquinone triphenylphosphonium derivs. as mitochondrially  
 targeted antioxidants)  
 RN 764723-90-2 CAPLUS  
 CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
 yl)pentyl]triphenyl-, iodide (1:1) (CA INDEX NAME)



RN 764723-92-4 CAPLUS  
 CN Phosphonium, [15-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
 yl)pentadecyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



RN 845959-58-2 CAPLUS  
 CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
 yl)propyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

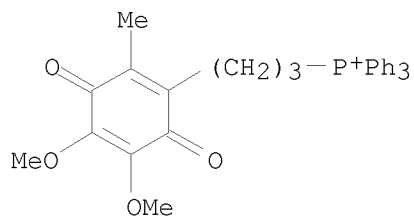
10568655

09/08/2010

STN: SEARCH

CRN 794485-93-1

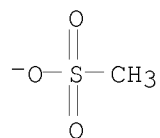
CMF C30 H30 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



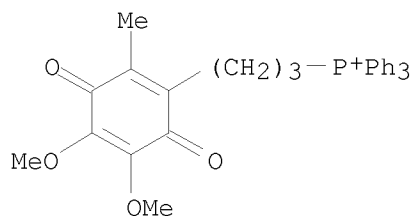
IT 845959-57-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of mitoquinone triphenylphosphonium derivs. as mitochondrially targeted antioxidants)

RN 845959-57-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



OS.CITING REF COUNT: 2

THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

L3 ANSWER 60 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN



ACCESSION NUMBER: 2006:202663 CAPLUS  
DOCUMENT NUMBER: 145:202743  
TITLE: The effects of exogenous antioxidants on lifespan and oxidative stress resistance in *Drosophila melanogaster*  
AUTHOR(S): Magwere, Tapiwanashe; West, Melanie; Riyahi, Kumars; Murphy, Michael P.; Smith, Robin A. J.; Partridge, Linda  
CORPORATE SOURCE: Centre for Research on Aging, Department of Biology, University College London, London, WC1E 6BT, UK  
SOURCE: Mechanisms of Ageing and Development (2006), 127(4), 356-370  
CODEN: MAGDA3; ISSN: 0047-6374  
PUBLISHER: Elsevier Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB We used the fruit fly *Drosophila melanogaster* to test the effects of feeding the superoxide dismutase (SOD) mimetic drugs Euk-8 and -134 and the mitochondria-targeted mitoquinone (MitoQ) on lifespan and oxidative stress resistance of wild type and SOD-deficient flies. Our results reaffirm the findings by other workers that exogenous antioxidant can rescue pathol. associated with compromised defences to oxidative stress, but fail to extend the lifespan of normal, wild type animals. All three drugs showed a dose-dependent increase in toxicity in wild type flies, an effect that was exacerbated in the presence of the redox-cycling drug paraquat. However, important findings from this study were that in SOD-deficient flies, where the antioxidant drugs increased lifespan, the effects were sex-specific and, for either sex, the effects were also variable depending on (1) the stage of development from which the drugs were given, and (2) the magnitude of the dose. These findings place significant constraints on the role of oxidative stress in normal aging.

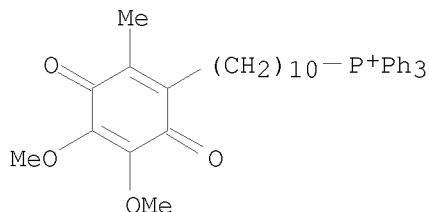
IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antioxidant drug, mitochondria-targeted mitoquinone dose-dependently increased toxicity in wild type flies while it increased lifespan in superoxide dismutase-deficient *Drosophila melanogaster*)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 38 THERE ARE 38 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)  
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 61 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:51133 CAPLUS  
 DOCUMENT NUMBER: 144:121851  
 TITLE: Use of mitochondrially targeted antioxidant-lipophilic cation conjugate in the treatment of liver diseases and epithelial cancers.  
 INVENTOR(S): Froehlich, Eleonore; Kvietikova, Ivica; Zatloukal, Kurt; Schatz, Gottfried; Denk, Helmut; Stumptner, Cornelia; Buck, Charles  
 PATENT ASSIGNEE(S): Oridis Biomed Forschungs- und Entwicklungs G.m.b.H., Austria  
 SOURCE: PCT Int. Appl., 61 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006005759	A2	20060119	WO 2005-EP53338	20050712
WO 2006005759	A3	20060511		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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CA 2573456	A1	20060119	CA 2005-2573456	20050712
EP 1765413	A2	20070328	EP 2005-775873	20050712
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
CN 1997403	A	20070711	CN 2005-80023193	20050712
JP 2008506667	T	20080306	JP 2007-520833	20050712
SG 156613	A1	20091126	SG 2009-6579	20050712
ZA 2006009635	A	20080827	ZA 2006-9635	20061120
KR 2007030815	A	20070316	KR 2006-725659	20061206
US 20070225255	A1	20070927	US 2007-632149	20070212
PRIORITY APPLN. INFO.:			EP 2004-103318	A 20040713
			WO 2005-EP53338	W 20050712

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 144:121851

AB The invention discloses the use of a mitochondrially targeted antioxidant, e.g. derivs. of vitamin E, coenzyme Q10 or a glutathione peroxidase mimetic, in the treatment and prevention of liver diseases and/or epithelial cancers. The invention also discloses pharmaceutical compns. containing the antioxidant(s) intended for such use. Furthermore the invention relates to the manufacture of medicaments containing the antioxidant(s) useful for such prevention and treatment. Compds. of the invention comprise a lipophilic cation covalently coupled to an antioxidant moiety,

e.g. (Ph)<sub>3</sub>P+XR·Z<sup>-</sup> (X = linking group; R = antioxidant moiety; Z<sup>-</sup> = anion).

IT 873653-01-1 873653-02-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitochondrially targeted antioxidant-lipophilic cation conjugate for treatment of liver disease and epithelial cancer)

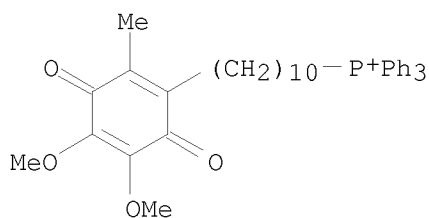
RN 873653-01-1 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide, mixt. with [10-(3,6-dihydroxy-4,5-dimethoxy-2-methylphenyl)decyl]triphenylphosphonium bromide (9CI) (CA INDEX NAME)

CM 1

CRN 336184-91-9

CMF C37 H44 O4 P . Br

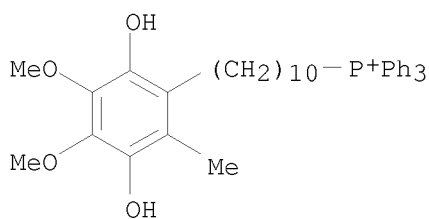


● Br<sup>-</sup>

CM 2

CRN 299975-19-2

CMF C37 H46 O4 P . Br



● Br<sup>-</sup>

RN 873653-02-2 CAPLUS

CN Phosphonium, [10-(3,6-dihydroxy-4,5-dimethoxy-2-methylphenyl)decyl]triphenyl-, methanesulfonate, mixt. with

[10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (9CI) (CA INDEX NAME)

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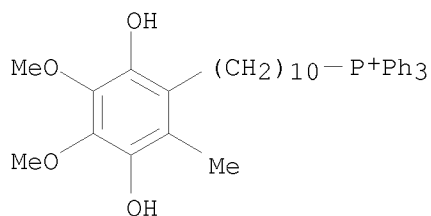
CRN 845959-55-9

CMF C37 H46 O4 P . C H3 O3 S

CM 2

CRN 747398-82-9

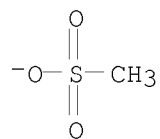
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CM 3

CRN 16053-58-0

CMF C H3 O3 S



CM 4

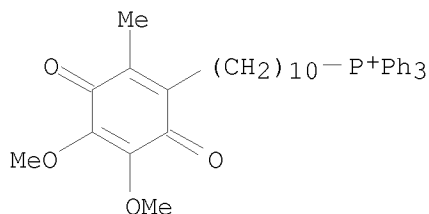
CRN 845959-50-4

CMF C37 H44 O4 P . C H3 O3 S

CM 5

CRN 444890-41-9

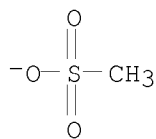
CMF C37 H44 O4 P



CM 6

CRN 16053-58-0

CMF C H3 O3 S



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 62 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:584282 CAPLUS

DOCUMENT NUMBER: 143:241657

TITLE: Targeting an antioxidant to mitochondria decreases cardiac ischemia-reperfusion injury

AUTHOR(S): Adlam, Victoria J.; Harrison, Joanne C.; Porteous, Carolyn M.; James, Andrew M.; Smith, Robin A. J.; Murphy, Michael P.; Sammut, Ivan A.

CORPORATE SOURCE: Department of Chemistry, University of Otago, Dunedin, N. Z.

SOURCE: FASEB Journal (2005), 19(9), 1088-1095

CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mitochondrial oxidative damage contributes to a wide range of pathologies, including cardiovascular disorders and neurodegenerative diseases. Therefore, protecting mitochondria from oxidative damage should be an effective therapeutic strategy. However, conventional antioxidants have limited efficacy due to the difficulty of delivering them to mitochondria in situ. To overcome this problem, we developed mitochondria-targeted antioxidants, typified by MitoQ, which comprises a lipophilic triphenylphosphonium (TPP) cation covalently attached to a ubiquinol antioxidant. Driven by the large mitochondrial membrane potential, the TPP cation concs. MitoQ several hundred-fold within mitochondria, selectively preventing mitochondrial oxidative damage. To test whether MitoQ was active in vivo, we chose a clin. relevant form of mitochondrial oxidative damage: cardiac ischemia-reperfusion injury. Feeding MitoQ to

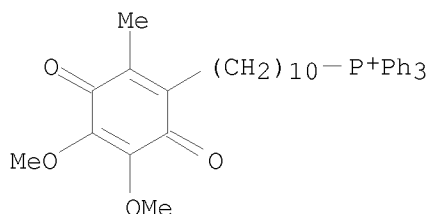
rats significantly decreased heart dysfunction, cell death, and mitochondrial damage after ischemia-reperfusion. This protection was due to the antioxidant activity of MitoQ within mitochondria, as an untargeted antioxidant was ineffective and accumulation of the TPP cation alone gave no protection. Therefore, targeting antioxidants to mitochondria in vivo is a promising new therapeutic strategy in the wide range of human diseases such as Parkinson's disease, diabetes, and Friedreich's ataxia where mitochondrial oxidative damage underlies the pathol.

IT 444890-41-9, MitoQ

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(targeting an antioxidant to mitochondria decreases cardiac ischemia-reperfusion injury)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 118 THERE ARE 118 CAPLUS RECORDS THAT CITE THIS RECORD (118 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 63 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:463624 CAPLUS

DOCUMENT NUMBER: 143:148390

TITLE: Interactions of Mitochondria-targeted and Untargeted Ubiquinones with the Mitochondrial Respiratory Chain and Reactive Oxygen Species: implications for the use of exogenous ubiquinones as therapies and experimental tools

AUTHOR(S): James, Andrew M.; Cocheme, Helena M.; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: Medical Research Council Dunn Human Nutrition Unit, Cambridge, CB2 2XY, UK

SOURCE: Journal of Biological Chemistry (2005), 280(22), 21295-21312

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antioxidants, such as ubiquinones, are widely used in mitochondrial studies as both potential therapies and useful research tools. However, the effects of exogenous ubiquinones can be difficult to interpret because they can also be pro-oxidants or electron carriers that facilitate respiration. Recently we developed a mitochondria-targeted ubiquinone

(MitoQ10) that accumulates within mitochondria. MitoQ10 has been used to prevent mitochondrial oxidative damage and to infer the involvement of mitochondrial reactive oxygen species in signaling pathways. However, uncertainties remain about the mitochondrial reduction of MitoQ10, its oxidation

by the respiratory chain, and its pro-oxidant potential. Therefore, we compared MitoQ analogs of varying alkyl chain lengths (MitoQn, n = 3-15) with untargeted exogenous ubiquinones. We found that MitoQ10 could not restore respiration in ubiquinone-deficient mitochondria because oxidation of MitoQ analogs by complex III was minimal. Complex II and glycerol 3-phosphate dehydrogenase reduced MitoQ analogs, and the rate depended on chain length. Because of its rapid reduction and negligible oxidation, MitoQ10 is a more effective antioxidant against lipid peroxidn., peroxynitrite and superoxide. Paradoxically, exogenous ubiquinols also autoxidize to generate superoxide, but this requires their deprotonation in the aqueous phase. Consequently, in the presence of phospholipid bilayers, the rate of autoxidn. is proportional to ubiquinol hydrophilicity. Superoxide production by MitoQ10 was insufficient to damage aconitase but did lead to hydrogen peroxide production and nitric oxide consumption, both of which may affect cell signaling pathways. Our results comprehensively describe the interaction of exogenous ubiquinones with mitochondria and have implications for their rational design and use as therapies and as research tools to probe mitochondrial function.

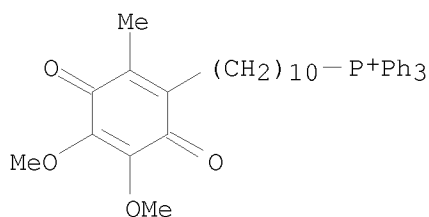
IT 444890-41-9 794485-93-1 794485-94-2  
794485-95-3

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(interactions of mitochondria-targeted and untargeted ubiquinones with the mitochondrial respiratory chain and reactive oxygen species)

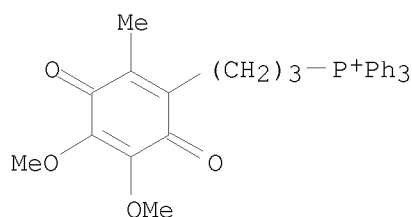
RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



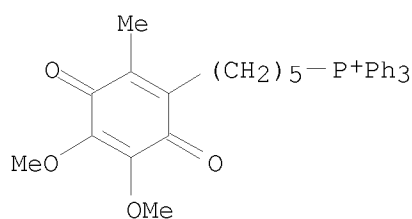
RN 794485-93-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl- (CA INDEX NAME)



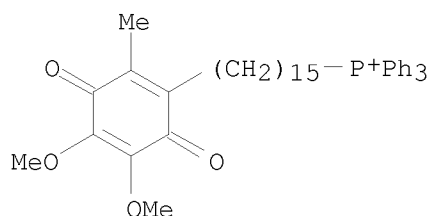
RN 794485-94-2 CAPLUS

CN	Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl- (CA INDEX NAME)
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RN 794485-95-3 CAPLUS

CN    Phosphonium, [15-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentadecyl]triphenyl- (CA INDEX NAME)



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OS.CITING REF COUNT:      87   THERE ARE 87 CAPLUS RECORDS THAT CITE THIS
                             RECORD (87 CITINGS)
REFERENCE COUNT:          95   THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS
                             RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L3 ANSWER 64 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:182678 CAPLUS

DOCUMENT NUMBER: 142:254662

TITLE: Mitouquinone derivatives used as mitochondrially targeted antioxidants, and preparation thereof

INVENTOR(S): Murphy, Michael Patrick; Smith, Robin  
PATENT ASSIGNEE(S): Antipodean Biotechnology Limited, N. Z.

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English



FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019233	A1	20050303	WO 2004-NZ197	20040823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NZ 547102	A	20090731	NZ 2003-547102	20030822
US 20070238709	A1	20071011	US 2007-568654	20070222
US 20080275005	A1	20081106	US 2008-109170	20080424

PRIORITY APPLN. INFO.:

NZ 2003-527800	A	20030822
NZ 2003-529153	A	20031023
NZ 2004-533555	A	20040614
WO 1998-NZ173	A2	19981125
US 2000-577877	A1	20000525
US 2001-968838	B1	20011003
US 2002-272914	B1	20021018
US 2003-722542	B1	20031128
NZ 2004-533556	A	20040614
WO 2004-NZ196	W	20040823
WO 2004-NZ197	W	20040823
US 2005-172916	A1	20050705
US 2006-568655	A2	20060831
US 2007-568654	A2	20070222
US 2007-799779	A2	20070502

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 142:254662; MARPAT 142:254662

AB This invention discloses methods to screen for, identify, select, and synthesize amphiphilic mitochondrially targeted antioxidant compds., and compns., dosage forms, and methods reliant on these compds. The compds. are all mitoquinone derivs., being methoxyphenyl alkyl triphenylphosphonium or methoxy dioxocyclohexadiene alkyl triphenylphosphonium derivs. The compds., compns., dosage forms and methods are useful in e.g. the treatment of diseases or conditions associated with oxidative stress.

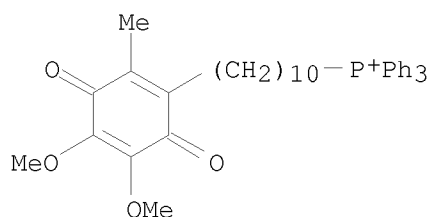
IT 444890-41-9 794485-93-1 794485-94-2

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

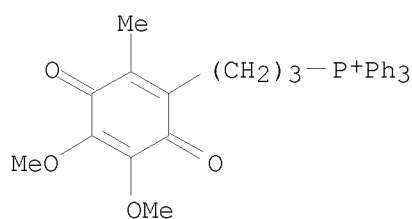
RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



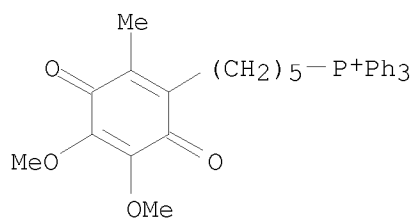
RN 794485-93-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl- (CA INDEX NAME)



RN 794485-94-2 CAPLUS

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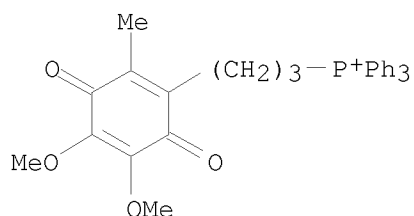
IT 845959-57-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

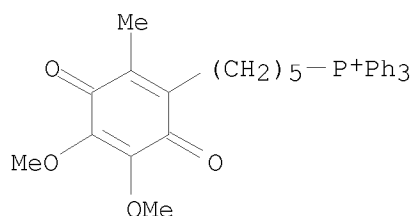
RN 845959-57-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



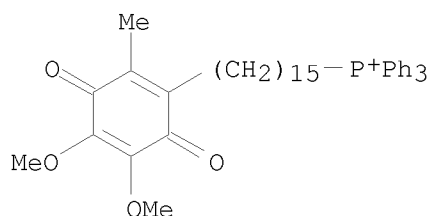
● Br<sup>-</sup>

IT 764723-90-2P 764723-92-4P 845959-58-2P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (mitoquinone derivative preparation for mitochondrially targeted  
 antioxidant)  
 RN 764723-90-2 CAPLUS  
 CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-  
 yl)pentyl]triphenyl-, iodide (1:1) (CA INDEX NAME)



● I<sup>-</sup>

RN 764723-92-4 CAPLUS  
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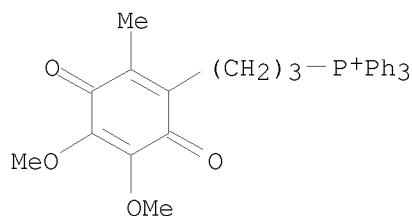
RN 845959-58-2 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

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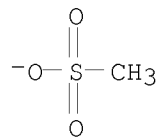
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CM 2

CRN 16053-58-0

CMF C H3 O3 S



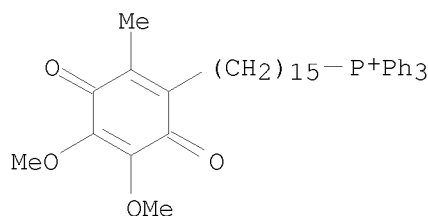
IT 794485-95-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

RN 794485-95-3 CAPLUS

CN Phosphonium, [15-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentadecyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
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REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 65 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:182677 CAPLUS

DOCUMENT NUMBER: 142:254661

TITLE: Mitoquinone derivatives used as mitochondrially  
targeted antioxidants, and preparation thereof

INVENTOR(S): Taylor, Kenneth Martin; Smith, Robin

PATENT ASSIGNEE(S): Antipodean Biotechnology Limited, N. Z.

SOURCE: PCT Int. Appl., 143 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019232	A1	20050303	WO 2004-NZ196	20040823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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			WO 1998-NZ173	A2 19981125
			US 2000-577877	A1 20000525
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			KR 2006-703665	A3 20060222
			US 2006-568655	A2 20060831
			US 2007-568654	A2 20070222
			US 2007-799779	A2 20070502

## ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 142:254661; MARPAT 142:254661

AB The invention discloses pharmaceutically acceptable amphiphilic antioxidant compds., compns., and dosage forms comprising these compds., and methods and uses reliant on these compds. The compds. are all mitoquinone derivs., being methoxyphenyl alkyl triphenylphosphonium or methoxy dioxocyclohexadiene alkyl triphenylphosphonium derivs. The compds., compns., dosage forms, uses, and methods are useful in e.g. the treatment of diseases or conditions associated with oxidative stress.

IT 845959-50-4P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

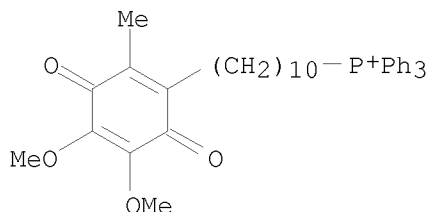
RN 845959-50-4 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 444890-41-9

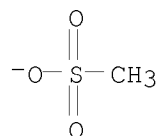
CMF C37 H44 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



IT 845959-59-3P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

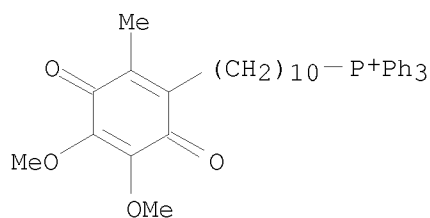
RN 845959-59-3 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 444890-41-9

CMF C37 H44 O4 P



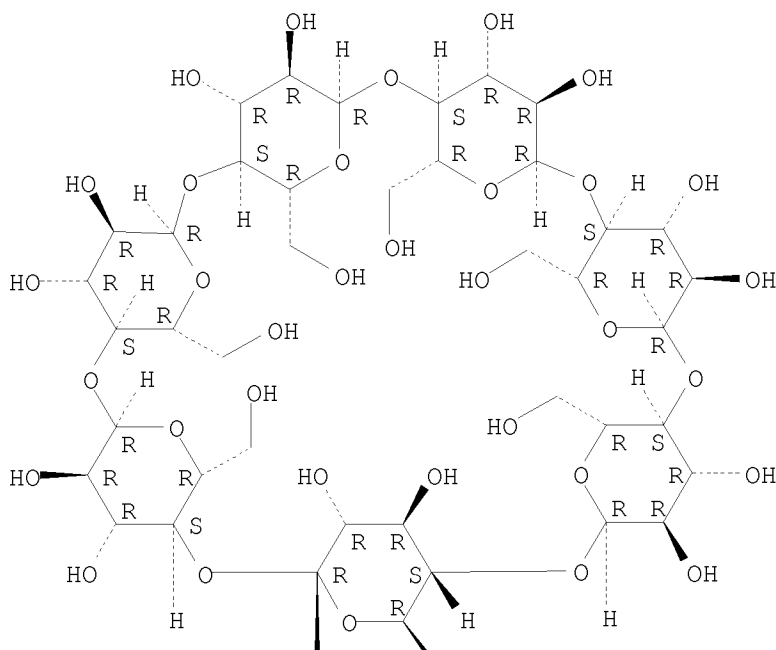
CM 2

CRN 7585-39-9

CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 764723-90-2P 764723-92-4P 845959-58-2P  
845959-60-6P

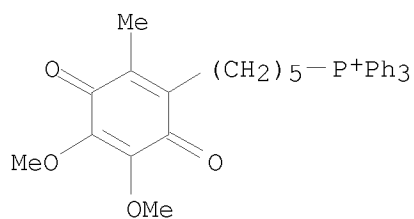
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

RN 764723-90-2 CAPLUS

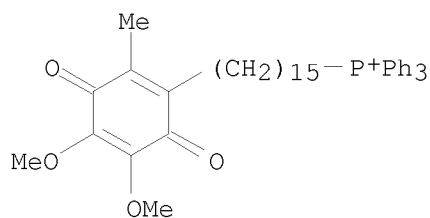
CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl-, iodide (1:1) (CA INDEX NAME)





RN 764723-92-4 CAPLUS

CN Phosphonium, [15-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentadecyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



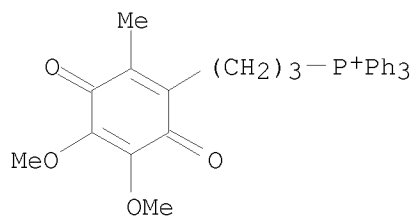
RN 845959-58-2 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 794485-93-1

CMF C30 H30 O4 P



CM 2

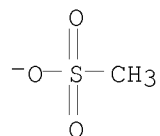
10568655

09/08/2010

STN: SEARCH

CRN 16053-58-0

CMF C H3 O3 S



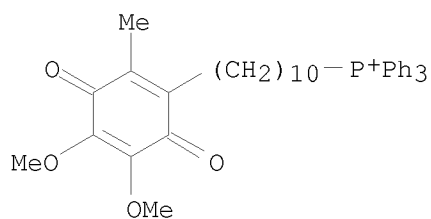
RN 845959-60-6 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium (4:1) (9CI) (CA INDEX NAME)

CM 1

CRN 444890-41-9

CMF C37 H44 O4 P



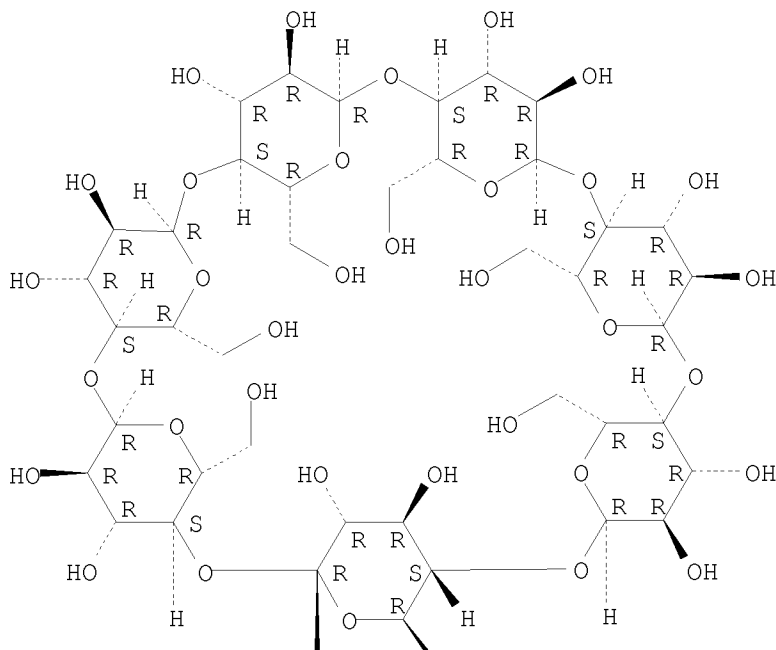
CM 2

CRN 7585-39-9

CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 845959-56-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

RN 845959-56-0 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (2:1) (9CI)  
(CA INDEX NAME)

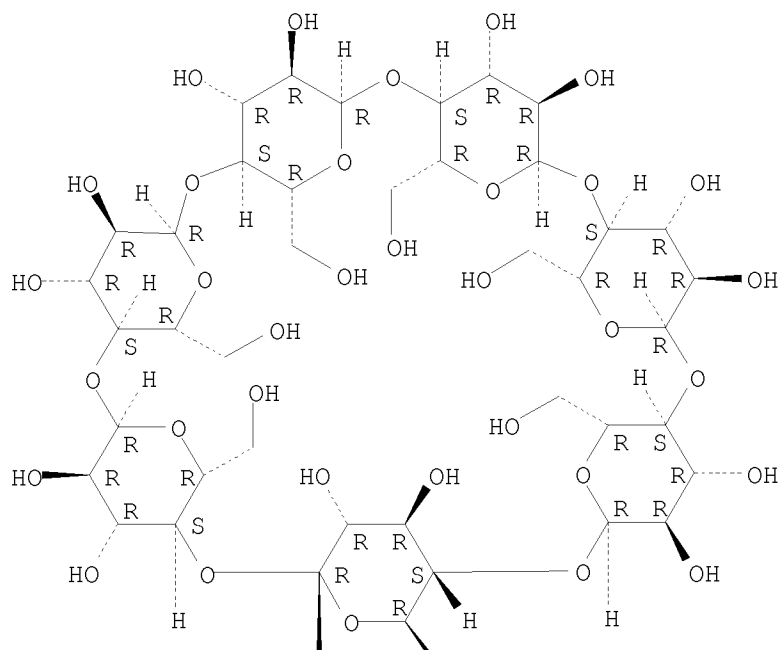
CM 1

CRN 7585-39-9

CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



CM 2

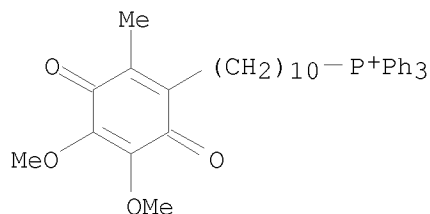
CRN 845959-50-4

CMF C37 H44 O4 P . C H3 O3 S

CM 3

CRN 444890-41-9

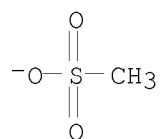
CMF C37 H44 O4 P



CM 4

CRN 16053-58-0

CMF C H3 O3 S



IT 444890-41-9 845959-51-5 845959-52-6

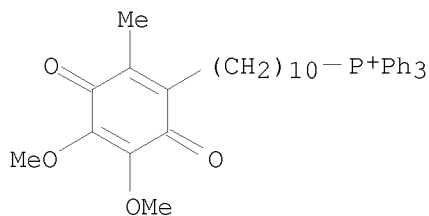
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



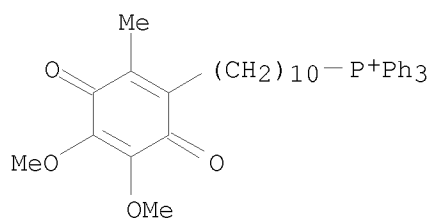
RN 845959-51-5 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenylphosphonium (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 444890-41-9

CMF C37 H44 O4 P



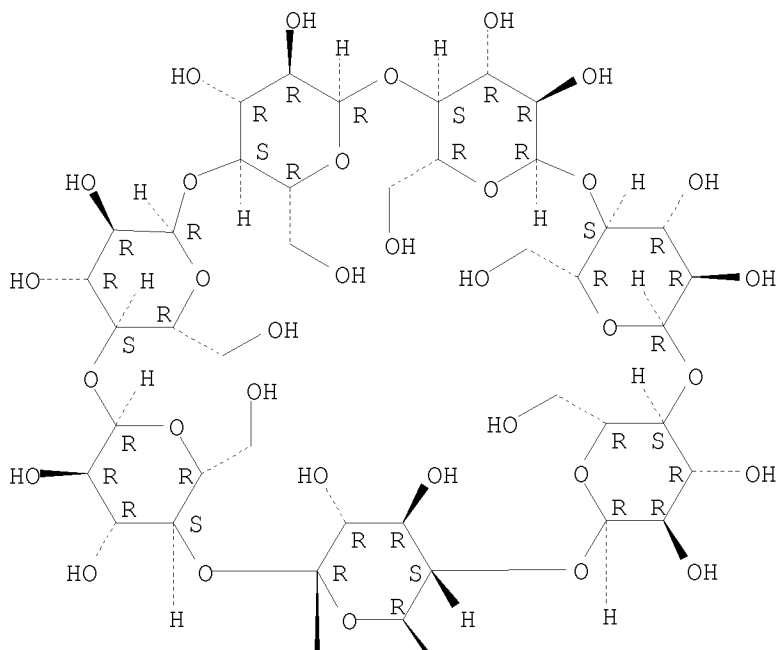
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CRN 7585-39-9

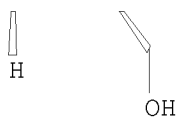
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



RN 845959-52-6 CAPLUS

CN  $\beta$ -Cyclodextrin, compd. with [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-

cyclohexadien-1-yl)decyl]triphenylphosphonium methanesulfonate (1:1) (9CI)  
(CA INDEX NAME)

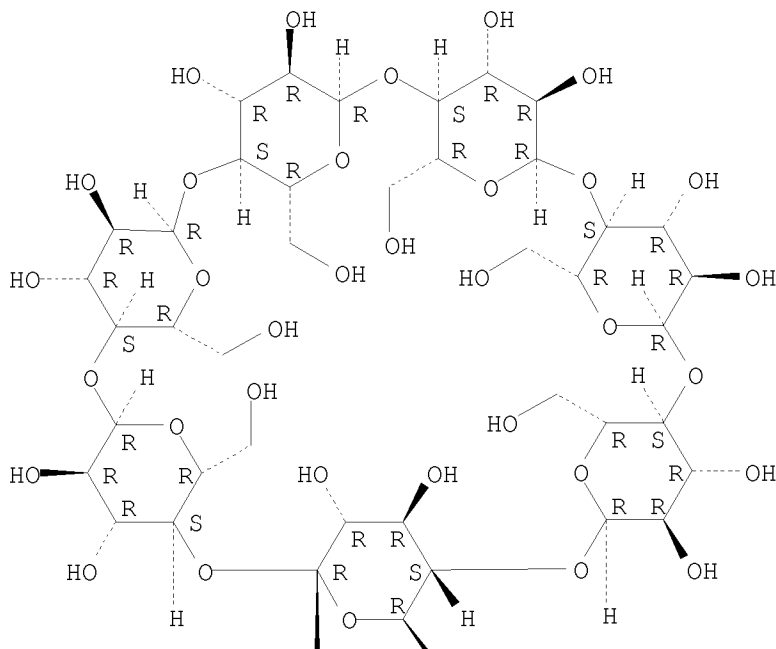
CM 1

CRN 7585-39-9

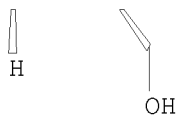
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



CM 2

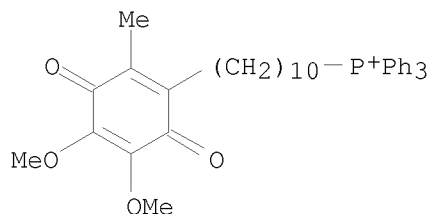
CRN 845959-50-4

CMF C37 H44 O4 P . C H3 O3 S

CM 3

CRN 444890-41-9

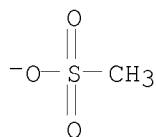
CMF C37 H44 O4 P



CM 4

CRN 16053-58-0

CMF C H3 O3 S



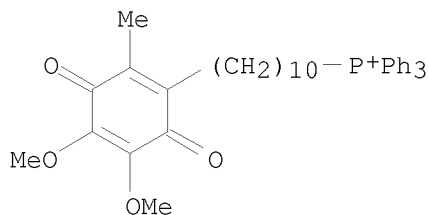
IT 336184-91-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)

● Br<sup>-</sup>

IT 845959-57-1P

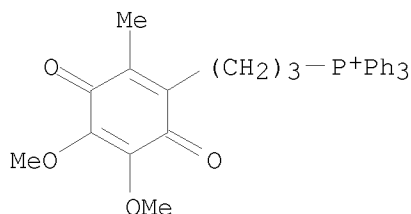
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(mitoquinone derivative preparation for mitochondrially targeted antioxidant)

RN 845959-57-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)





● Br<sup>-</sup>

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)  
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 66 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:710408 CAPLUS

DOCUMENT NUMBER: 141:236523

TITLE: Supplementation of Endothelial Cells with Mitochondria-targeted Antioxidants Inhibit Peroxide-induced Mitochondrial Iron Uptake, Oxidative Damage, and Apoptosis

AUTHOR(S): Dhanasekaran, Anuradha; Kotamraju, Srigiridhar; Kalivendi, Shasi V.; Matsunaga, Toshiyuki; Shang, Tiesong; Keszler, Agnes; Joseph, Joy; Kalyanaraman, B.  
CORPORATE SOURCE: Department of Biophysics and Free Radical Research Center, Medical College of Wisconsin, Milwaukee, WI, 53226, USA

SOURCE: Journal of Biological Chemistry (2004), 279(36), 37575-37587

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mitochondria-targeted drugs mitoquinone (Mito-Q) and mitovitamin E (MitoVit-E) are a new class of antioxidants containing the triphenylphosphonium cation moiety that facilitates drug accumulation in mitochondria. In this study, Mito-Q (ubiquinone attached to a triphenylphosphonium cation) and MitoVit-E (vitamin E attached to a triphenylphosphonium cation) were used. The aim of this study was to test the hypothesis that mitochondria-targeted antioxidants inhibit peroxide-induced oxidative stress and apoptosis in bovine aortic endothelial cells (BAEC) through enhanced scavenging of mitochondrial reactive oxygen species, thereby blocking reactive oxygen species-induced transferrin receptor (TfR)-mediated iron uptake into mitochondria. Glucose/glucose oxidase-induced oxidative stress in BAECs was monitored by oxidation of dichlorodihydrofluorescein that was catalyzed by both intracellular H<sub>2</sub>O<sub>2</sub> and transferrin iron transported into cells. Pretreatment of BAECs with Mito-Q (1 μM) and MitoVit-E (1 μM) but not untargeted antioxidants (e.g. vitamin E) significantly abrogated H<sub>2</sub>O<sub>2</sub>- and lipid peroxide-induced 2',7'-dichlorofluorescein fluorescence and

protein oxidation Mitochondria-targeted antioxidants inhibit cytochrome c release, caspase-3 activation, and DNA fragmentation. Mito-Q and MitoVit-E inhibited H<sub>2</sub>O<sub>2</sub>- and lipid peroxide-induced inactivation of complex I and aconitase, TfR overexpression, and mitochondrial uptake of <sup>55</sup>Fe, while restoring the mitochondrial membrane potential and proteasomal activity. The authors conclude that Mito-Q or MitoVit-E supplementation of endothelial cells mitigates peroxide-mediated oxidant stress and maintains proteasomal function, resulting in the overall inhibition of TfR-dependent iron uptake and apoptosis.

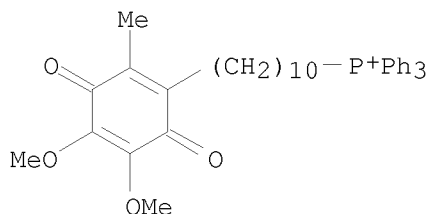
IT 336184-91-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(supplementation of endothelial cells with mitochondria-targeted antioxidants inhibit peroxide-induced mitochondrial iron uptake, oxidative damage, and apoptosis)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



OS.CITING REF COUNT: 77 THERE ARE 77 CAPLUS RECORDS THAT CITE THIS RECORD (77 CITINGS)  
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 67 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:601038 CAPLUS

DOCUMENT NUMBER: 141:290668

TITLE: Fine-tuning the hydrophobicity of a mitochondria-targeted antioxidant

AUTHOR(S): Asin-Cayuela, Jordi; Manas, Abdul-Rahman B.; James, Andrew M.; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: Wellcome Trust/MRC Building, Medical Research Council Dunn Human Nutrition Unit, Cambridge, CB2 2XY, UK

SOURCE: FEBS Letters (2004), 571(1-3), 9-16  
CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

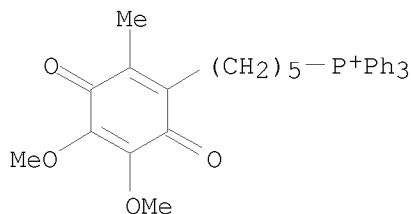
LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:290668

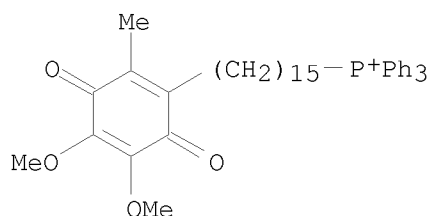
AB The mitochondria-targeted antioxidant MitoQ comprises a ubiquinol moiety covalently attached through an aliphatic carbon chain to the lipophilic triphenylphosphonium cation. This cation drives the membrane

potential-dependent accumulation of MitoQ into mitochondria, enabling the ubiquinol antioxidant to prevent mitochondrial oxidative damage far more effectively than untargeted antioxidants. We sought to fine-tune the hydrophobicity of MitoQ so as to control the extent of its membrane binding and penetration into the phospholipid bilayer, and thereby regulate its partitioning between the membrane and aqueous phases within mitochondria and cells. To do this, MitoQ variants with 3, 5, 10 and 15 carbon aliphatic chains were synthesized. These mols. had a wide range of hydrophobicities with octan-1-ol/phosphate buffered saline partition coeffs. from 2.8 to 20,000. All MitoQ variants were accumulated into mitochondria driven by the membrane potential, but their binding to phospholipid bilayers varied from negligible for MitoQ3 to essentially total for MitoQ15. Despite the span of hydrophobicities, all MitoQ variants were effective antioxidants. Therefore, it is possible to fine-tune the degree of membrane association of MitoQ and other mitochondria targeted compds., without losing antioxidant efficacy. This indicates how the uptake and distribution of mitochondria-targeted compds. within mitochondria and cells can be controlled, thereby facilitating investigations of mitochondrial oxidative damage.

IT 764723-90-2P 764723-92-4P 845959-57-1P  
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation of MitoQ variants for fine-tuning the hydrophobicity of a mitochondria-targeted antioxidant)  
RN 764723-90-2 CAPLUS  
CN Phosphonium, [5-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentyl]triphenyl-, iodide (1:1) (CA INDEX NAME)

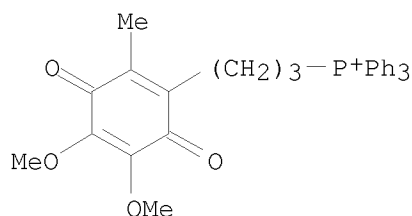


RN 764723-92-4 CAPLUS  
CN Phosphonium, [15-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)pentadecyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



RN 845959-57-1 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



IT 845959-58-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of MitoQ variants for fine-tuning the hydrophobicity of a mitochondria-targeted antioxidant)

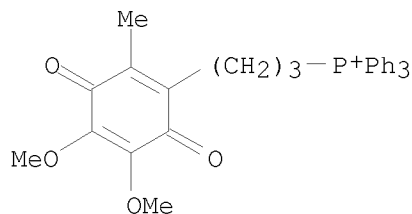
RN 845959-58-2 CAPLUS

CN Phosphonium, [3-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)propyl]triphenyl-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 794485-93-1

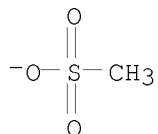
CMF C30 H30 O4 P



CM 2

CRN 16053-58-0

CMF C H3 O3 S



OS.CITING REF COUNT: 49 THERE ARE 49 CAPLUS RECORDS THAT CITE THIS  
RECORD (49 CITINGS)  
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 68 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:434607 CAPLUS

DOCUMENT NUMBER: 141:49659

TITLE: Mitochondria-derived reactive oxygen species mediate  
blue light-induced death of retinal pigment epithelial  
cellsAUTHOR(S): King, Ayala; Gottlieb, Eyal; Brooks, David G.; Murphy,  
Michael P.; Dunaief, Joshua L.CORPORATE SOURCE: F.M. Kirby Center for Molecular Ophthalmology, Scheie  
Eye Institute, University of Pennsylvania,  
Philadelphia, PA, USASOURCE: Photochemistry and Photobiology (2004), 79(5), 470-475  
CODEN: PHCBAP; ISSN: 0031-8655

PUBLISHER: American Society for Photobiology

DOCUMENT TYPE: Journal

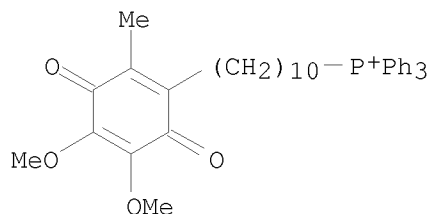
LANGUAGE: English

AB Throughout the lifetime of an individual, light is focused onto the retina. The resulting photooxidative stress can cause acute or chronic retinal damage. The pathogenesis of age-related macular degeneration (AMD), the leading cause of legal blindness in the developed world, involves oxidative stress and death of the retinal pigment epithelium (RPE) followed by death of the overlying photoreceptors. Evidence suggests that damage due to exposure to light plays a role in AMD and other age-related eye diseases. In this work a system for light-induced damage and death of the RPE, based on the human ARPE-19 cell line, was used. Induction of mitochondria-derived reactive oxygen species (ROS) is shown to play a critical role in the death of cells exposed to short-wavelength blue light (425 ± 20 nm). ROS and cell death are blocked either by inhibiting the mitochondrial electron transport chain or by mitochondria-specific antioxidants. These results show that mitochondria are an important source of toxic oxygen radicals in blue light-exposed RPE cells and may indicate new approaches for treating AMD using mitochondria-targeted antioxidants.

IT 336184-91-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mitochondria-derived ROS mediate blue light-induced death of retinal pigment epithelium)

RN 336184-91-9 CAPLUS  
CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)  
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 69 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:826167 CAPLUS

DOCUMENT NUMBER: 140:53354

TITLE: Mitochondria-targeted antioxidants protect Friedreich Ataxia fibroblasts from endogenous oxidative stress more effectively than untargeted antioxidants

AUTHOR(S): Jauslin, Matthias L.; Meier, Thomas; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: MyoContract Ltd., Liestal, CH-4410, Switz.

SOURCE: FASEB Journal (2003), 17(13), 1972-1974, 10.1096/fj.03-0240fje

CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

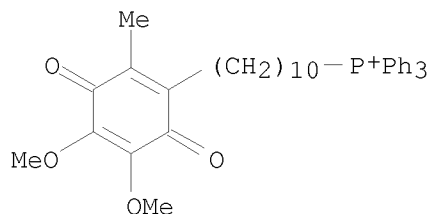
AB Friedreich Ataxia (FRDA), the most common inherited ataxia, arises from defective expression of the mitochondrial protein frataxin, which leads to increased mitochondrial oxidative damage. Therefore, antioxidants targeted to mitochondria should be particularly effective at slowing disease progression. To test this hypothesis, we compared the efficacy of mitochondria-targeted and untargeted antioxidants derived from coenzyme Q10 and from vitamin E at preventing cell death due to endogenous oxidative stress in cultured fibroblasts from FRDA patients in which glutathione synthesis was blocked. The mitochondria-targeted antioxidant MitoQ was several hundredfold more potent than the untargeted analog idebenone. The mitochondria-targeted antioxidant MitoVit E was 350-fold more potent than the water soluble analog Trolox. This is the first demonstration that mitochondria-targeted antioxidants prevent cell death that arises in response to endogenous oxidative damage. Targeted antioxidants may have therapeutic potential in FRDA and in other disorders involving mitochondrial oxidative damage.

IT 444890-41-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mitochondria-targeted antioxidants protect Friedreich Ataxia fibroblasts from endogenous oxidative stress more effectively than untargeted antioxidants)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 137 THERE ARE 137 CAPLUS RECORDS THAT CITE THIS RECORD (137 CITINGS)  
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 70 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:426934 CAPLUS

DOCUMENT NUMBER: 140:74526

TITLE: MitoQ counteracts telomere shortening and elongates lifespan of fibroblasts under mild oxidative stress

AUTHOR(S): Saretzki, Gabriele; Murphy, Michael P.; von Zglinicki, Thomas

CORPORATE SOURCE: Gerontology, Institute of Aging and Health, Newcastle University, Newcastle upon Tyne, NE4 6BE, UK

SOURCE: Aging Cell (2003), 2(2), 141-143

CODEN: ACGECQ; ISSN: 1474-9718

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

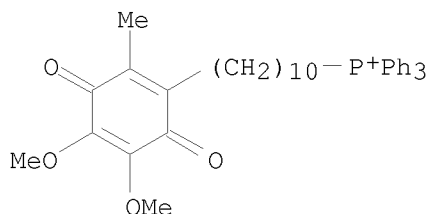
AB The effect of the mitochondria-specific antioxidant mitoQ [10-(6'-ubiquinonyl) decyltriphenylphosphonium bromide] in human fibroblasts under mild stress conditions was investigated. Treatment of MRC-5 fibroblasts with mitoQ under these conditions significantly decreased the cellular peroxide content and elongated the replicative lifespan. MitoQ treatment completely prevented the rise in telomere shortening rate due to hyperoxia and instead gave a negligible rate of telomere shortening.

IT 336184-91-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(MitoQ counteracts telomere shortening and elongates lifespan of human fibroblasts under mild oxidative stress)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



● Br<sup>-</sup>

OS.CITING REF COUNT: 50 THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (50 CITINGS)  
 REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 71 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:154438 CAPLUS

DOCUMENT NUMBER: 138:187926

TITLE: Preparation of triphenylphosphonium quinols and quinones

INVENTOR(S): Smith, Robin; Murphy, Michael Patrick

PATENT ASSIGNEE(S): Antipodean Biotechnology Limited, N. Z.

SOURCE: PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

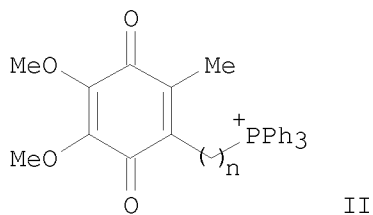
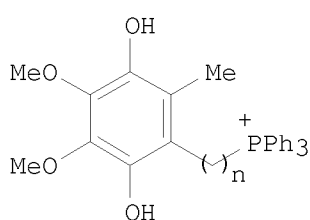
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016323	A1	20030227	WO 2002-NZ154	20020812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NZ 513547	A	20020927	NZ 2001-513547	20010813
AU 2002326242	A1	20030303	AU 2002-326242	20020812
EP 1423396	A1	20040602	EP 2002-760924	20020812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20050043553	A1	20050224	US 2004-486797	20041001
US 7179928	B2	20070220		
PRIORITY APPLN. INFO.:			NZ 2001-513547	A 20010813
			WO 2002-NZ154	W 20020812

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT



OTHER SOURCE(S):  
GI

CASREACT 138:187926; MARPAT 138:187926



AB Triphenylphosphonium quinols and quinones [e.g., I and II, resp.; wherein n = integer from 6 to 40] were prepared For example, Idebenone is reacted with PPh<sub>3</sub> and PPh<sub>3</sub>•HBr to give 57% MitoQuinol I Br<sup>-</sup> (n = 10), which is purified and oxidized with H<sub>2</sub>O<sub>2</sub>/pyridine to give 77% MitoQuinone II Br<sup>-</sup> (n = 10).

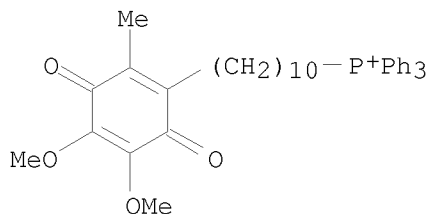
IT 336184-91-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of triphenylphosphonium quinols and quinones)

RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)



● Br<sup>-</sup>

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 72 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2002:411988 CAPLUS

DOCUMENT NUMBER: 137:139797

TITLE: Prevention of mitochondrial oxidative damage using targeted antioxidants

AUTHOR(S): Kelso, Geoffrey F.; Porteous, Carolyn M.; Hughes, Gillian; Ledgerwood, Elizabeth C.; Gane, Alison M.; Smith, Robin A. J.; Murphy, Michael P.

CORPORATE SOURCE: Departments of Chemistry, University of Otago,

SOURCE: Dunedin, N. Z.  
Annals of the New York Academy of Sciences (2002),  
959(Increasing Health Life Span), 263-274  
CODEN: ANYAA9; ISSN: 0077-8923  
PUBLISHER: New York Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Two mitochondria-targeted antioxidants that can selectively block mitochondrial oxidative damage and prevent some types of cell death were developed. They were ubiquinone and tocopherol derivs. targeted to mitochondria by covalent attachment to the lipophilic triphenylphosphonium cation. The effects of the 2 derivs. and nontargeted ubiquinone and tocopherol were examined in vitro in rat liver and beef heart mitochondrial preps. and in Jurkat human T lymphocyte cell line and in vivo in female Swiss Webster mice. Because of the large mitochondrial membrane potential, these cations can accumulated within mitochondria inside the cells, where the antioxidant moiety prevented lipid peroxidn. and protected the mitochondria from oxidative damage. The mitochondrially localized ubiquinone derivative also protected mammalian cells from hydrogen peroxide-induced apoptosis while the nontargeted ubiquinone analog was ineffective against cell apoptosis. When fed to mice, the 2 derivs. accumulated in the brain, heart, and liver. These mitochondria-targeted antioxidants may help in investigations of the role of mitochondrial oxidative damage in animal models of aging.

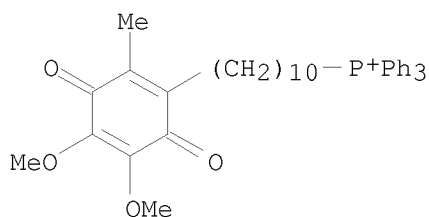
IT 444890-41-9

RL: BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(dietary ubiquinone and tocopherol targeted antioxidant derivs. use in prevention of mitochondrial oxidative damage in vitro and in mice)

RN 444890-41-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 59 THERE ARE 59 CAPLUS RECORDS THAT CITE THIS RECORD (59 CITINGS)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 73 OF 73 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:137933 CAPLUS

DOCUMENT NUMBER: 134:322127

TITLE: Selective targeting of a redox-active ubiquinone to mitochondria within cells. Antioxidant and antiapoptotic properties

AUTHOR(S): Kelso, Geoffrey F.; Porteous, Carolyn M.; Coulter, Carolyn V.; Hughes, Gillian; Porteous, William K.;

Ledgerwood, Elizabeth C.; Smith, Robin A. J.; Murphy, Michael P.  
CORPORATE SOURCE: Department of Chemistry, University of Otago, Dunedin, N. Z.  
SOURCE: Journal of Biological Chemistry (2001), 276(7), 4588-4596  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 134:322127

AB With the recognition of the central role of mitochondria in apoptosis, there is a need to develop specific tools to manipulate mitochondrial function within cells. Here we report on the development of a novel antioxidant that selectively blocks mitochondrial oxidative damage, enabling the roles of mitochondrial oxidative stress in different types of cell death to be inferred. This antioxidant, named mitoQ, is a ubiquinone derivative targeted to mitochondria by covalent attachment to a lipophilic triphenylphosphonium cation through an aliphatic carbon chain. Due to the large mitochondrial membrane potential, the cation was accumulated within mitochondria inside cells, where the ubiquinone moiety inserted into the lipid bilayer and was reduced by the respiratory chain. The ubiquinol derivative thus formed was an effective antioxidant that prevented lipid peroxidn. and protected mitochondria from oxidative damage. After detoxifying the reactive oxygen species peroxynitrite, the ubiquinol moiety was regenerated by the respiratory chain enabling its antioxidant activity to be recycled. In cell culture studies, the mitochondrially localized antioxidant protected mammalian cells from hydrogen peroxide-induced apoptosis but not from apoptosis induced by staurosporine or tumor necrosis factor- $\alpha$ . This was compared with untargeted ubiquinone analogs, which were ineffective in preventing apoptosis. These results suggest that mitochondrial oxidative stress may be a critical step in apoptosis induced by hydrogen peroxide but not for apoptosis induced by staurosporine or tumor necrosis factor- $\alpha$ . We have shown that selectively manipulating mitochondrial antioxidant status with targeted and recyclable antioxidants is a feasible approach to investigate the role of mitochondrial oxidative damage in apoptotic cell death. This approach will have further applications in investigating mitochondrial dysfunction in a range of exptl. models.

IT 336184-91-9P 336184-92-0P  
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(novel redox-active ubiquinone mitoQ displays antioxidant and antiapoptotic properties in mitochondria)

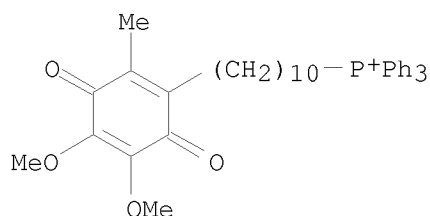
RN 336184-91-9 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1) (CA INDEX NAME)

10568655

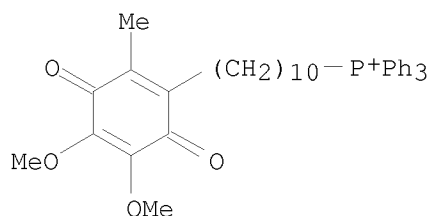
09/08/2010

STN: SEARCH

● Br<sup>-</sup>

RN 336184-92-0 CAPLUS

CN Phosphonium, [10-(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)decyl]triphenyl-, bromide (1:1), labeled with tritium (CA INDEX NAME)

● Br<sup>-</sup>

OS.CITING REF COUNT: 259 THERE ARE 259 CAPLUS RECORDS THAT CITE THIS RECORD (259 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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---Logging off of STN---

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	426.13	619.04
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

10568655 09/08/2010 STN: SEARCH

	ENTRY	SESSION
CA SUBSCRIBER PRICE	-62.05	-62.05

STN INTERNATIONAL LOGOFF AT 12:52:08 ON 08 SEP 2010